Unit 3.1

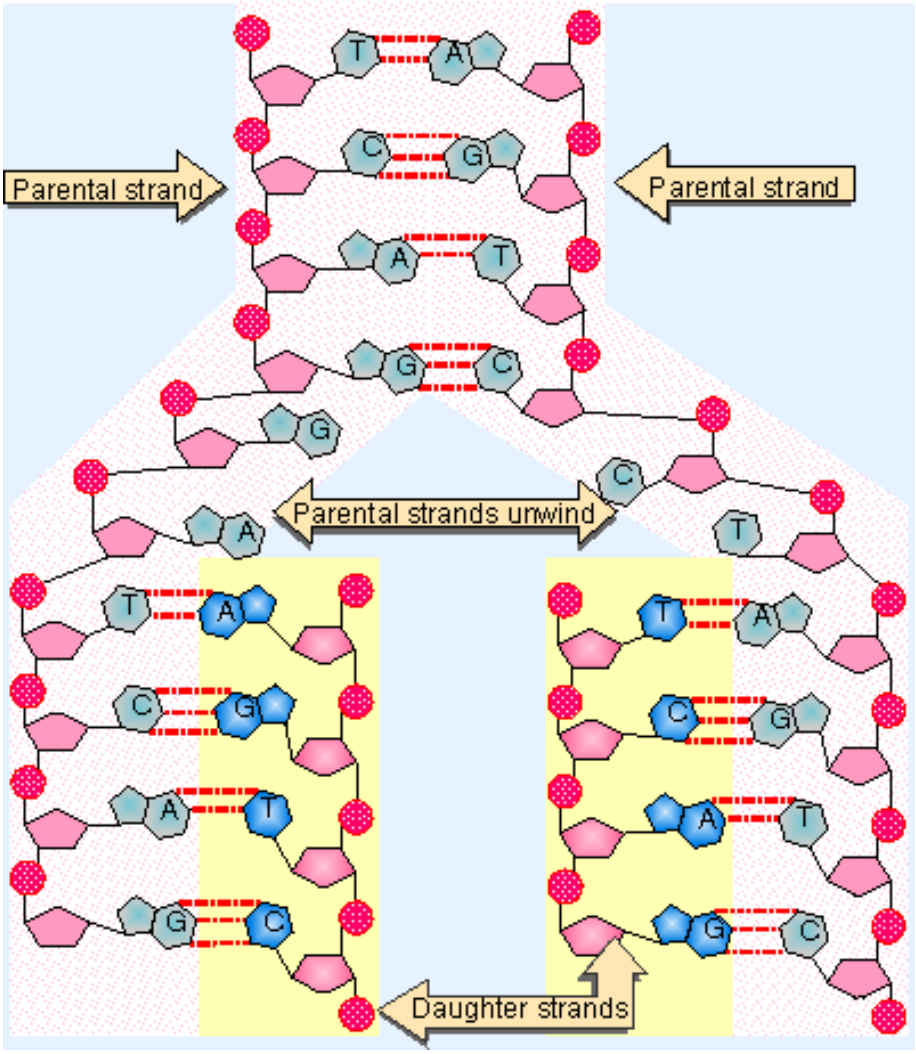
The Molecular Basis of Heredity – Genetic Information Systems

AP Biology

Mrs. Petrov

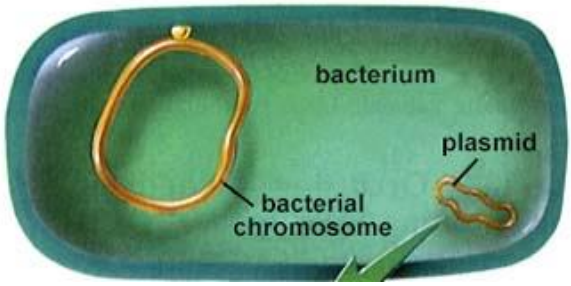
DNA

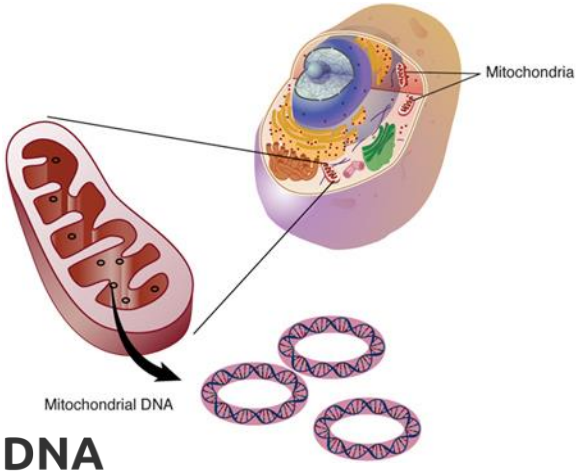
- DNA is the primary source of heritable information in most living things.
- The structure of nucleotide monomers allows for variation.
- DNA structure allows for **storage** of this genetic information with access to use it & replicate it when needed.

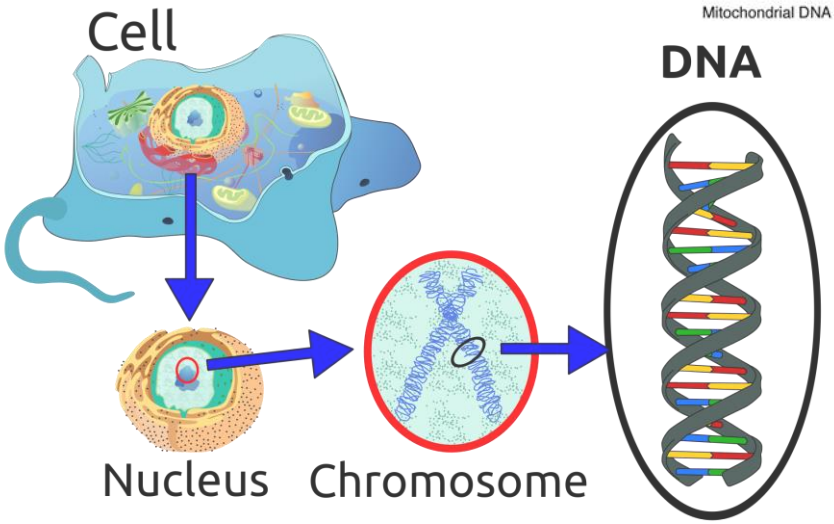


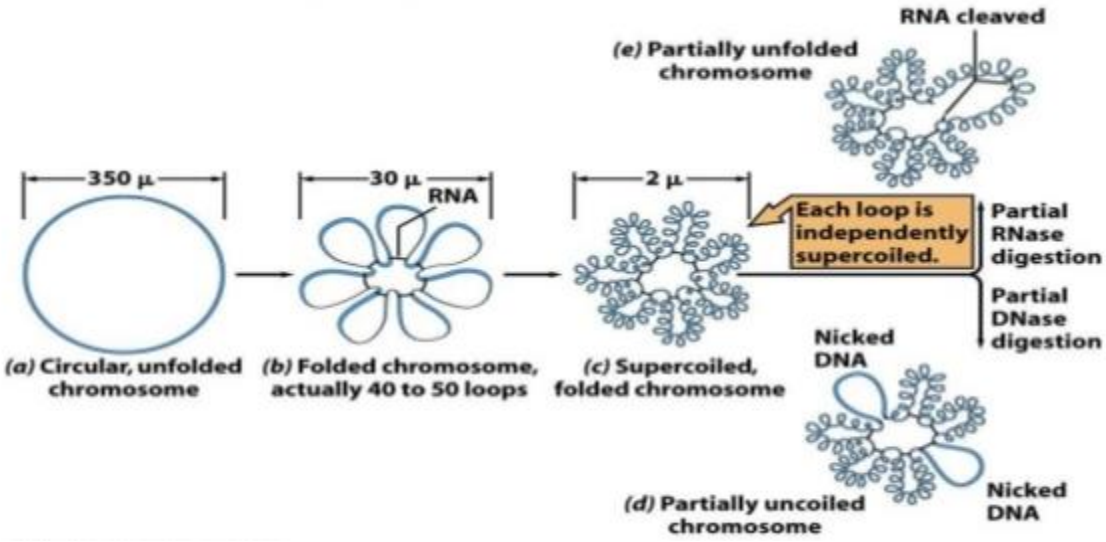
Chromosomes are DNA

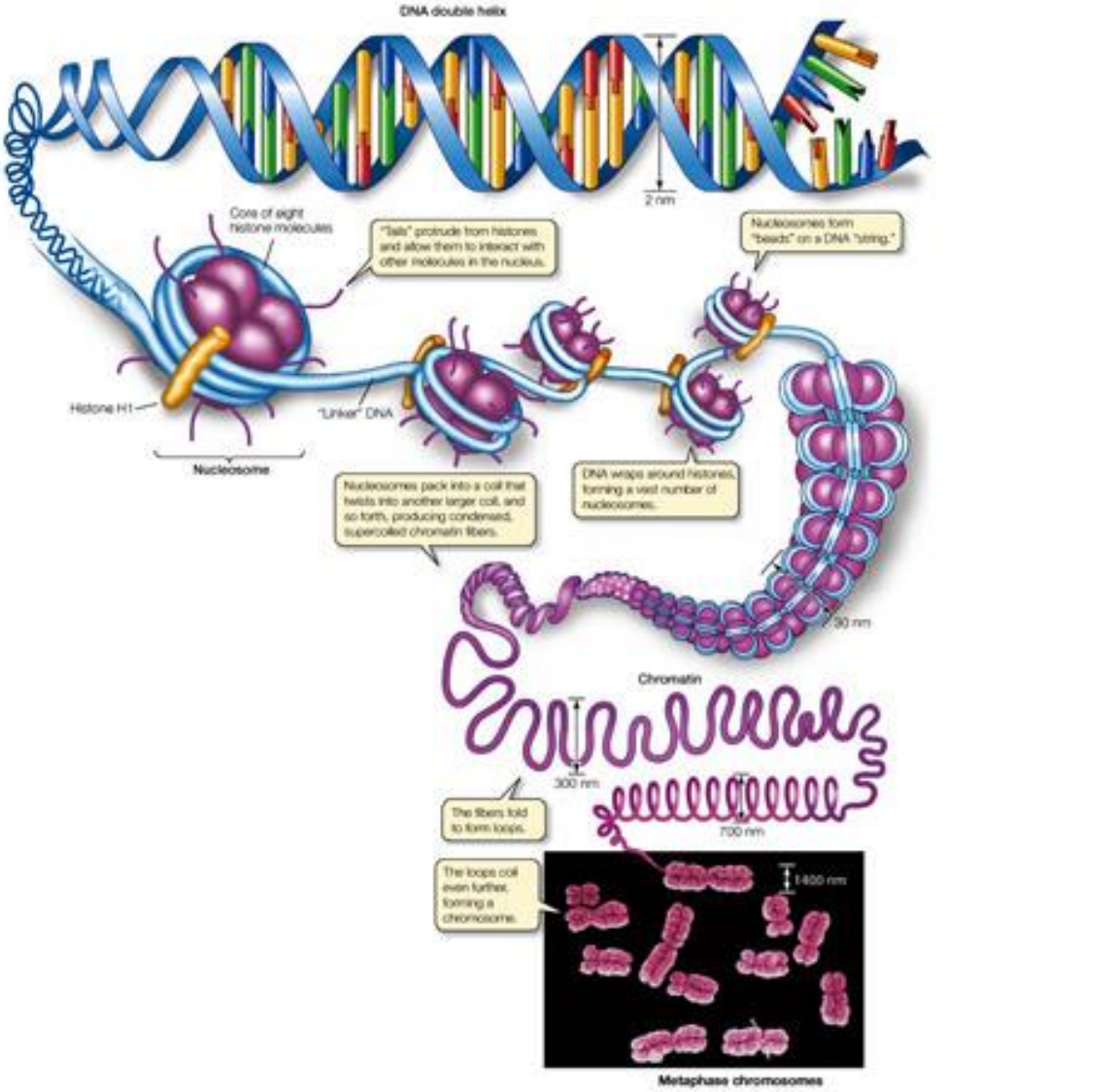
- Eukaryotes have **multiple linear chromosomes** in the nucleus.
  - **Circular** DNA in Mitochondria & Chloroplasts
- Prokaryotes & Viruses have **circular** chromosomes
- Many prokaryotes also have **plasmids**
  - Small, circular DNA molecules, separate from chromosome(s)








RNA cleaved
(e) Partially unfolded chromosome
350 μ
30 μ
RNA
2 μ
Each loop is independently supercoiled.
Partial RNase digestion
Partial DNase digestion
Nicked DNA
(a) Circular, unfolded chromosome
(b) Folded chromosome, actually 40 to 50 loops
(c) Supercoiled, folded chromosome
(d) Partially uncoiled chromosome
Nicked DNA


DNA double helix
2 nm
Core of eight histone molecules
"Tails" protrude from histones and allow them to interact with other molecules in the nucleus.
Nucleosomes form "beads" on a DNA "string."
Histone H1
"Linker" DNA
Nucleosome
Nucleosomes pack into a coil that twists into another larger coil, and so forth, producing condensed, supercoiled chromatin fibers.
DNA wraps around histones, forming a vast number of nucleosomes.
30 nm
Chromatin
300 nm
The fibers fold to form loops.
700 nm
The loops coil even further, forming a chromosome.
1400 nm
Metaphase chromosomes

1. The endosymbiotic theory states that many organelles, such as mitochondria, evolved as independent free-living prokaryotes that formed symbiotic relationships with other prokaryotes. The mitochondrion-like prokaryotes were engulfed but not digested by the other cells and performed vital energy conversions, while receiving protection by being inside the other cell. Which of the following provides the most accurate evidence in support of this theory?

    a. Mitochondria today have the same genes as prokaryotes today.
    b. The chromosome shape of mitochondrial DNA is similar to prokaryote DNA with many genes having more similar sequences to each other than the organelle DNA with its nuclear DNA.
    c. The products of cellular respiration in prokaryotes are identical to those in eukaryotes.
    d. The mitochondrial DNA has a similar shape to the prokaryote DNA and both have identical genes for producing their cell walls.

Nucleotides are the Building Blocks

- All have a phosphate, 5-carbon sugar, and a nitrogen base.
- RNA has ribose, DNA has deoxyribose.
- DNA has ATGC nitrogen bases, RNA has AUGC nitrogen bases.

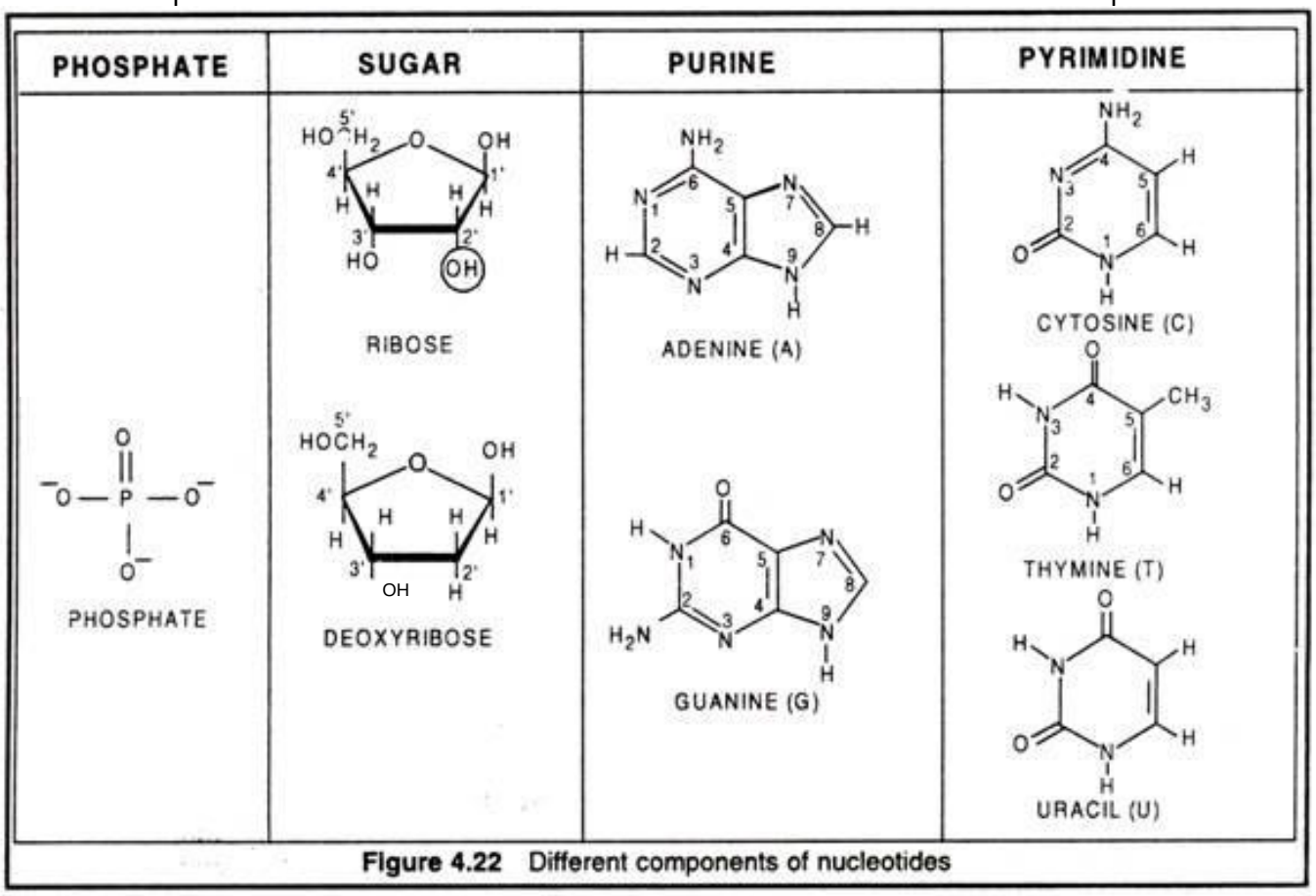


Figure 4.22 Different components of nucleotides

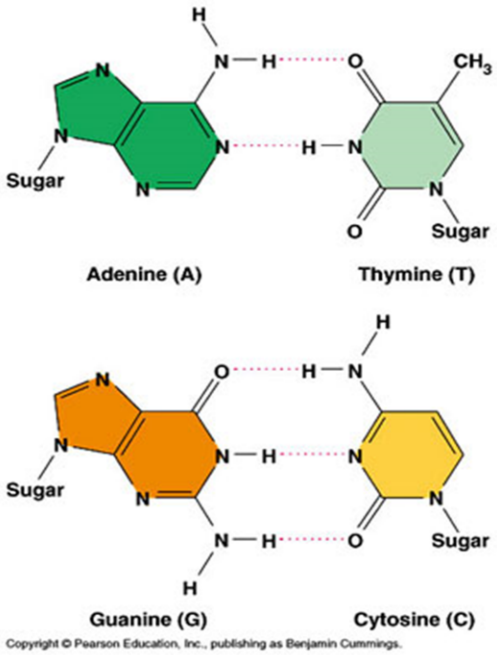
Base Pairing

Adenine pairs with Thymine (DNA) or Uracil (RNA)

-2 Hydrogen bonds

Guanine pairs with Cytosine

-3 Hydrogen bonds



Consider the following DNA sequences; which would be more stable & why?

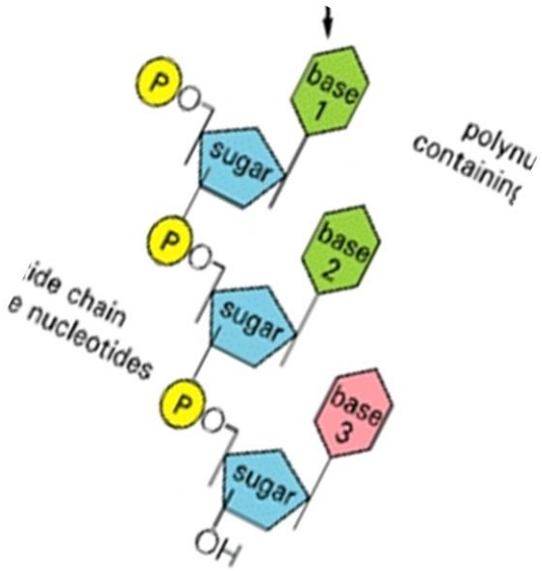
AAGGGTTTACATAAATATTTAAGGACGATGA
TTCCCAAATGTATTTATAAATTCCTGCTACT

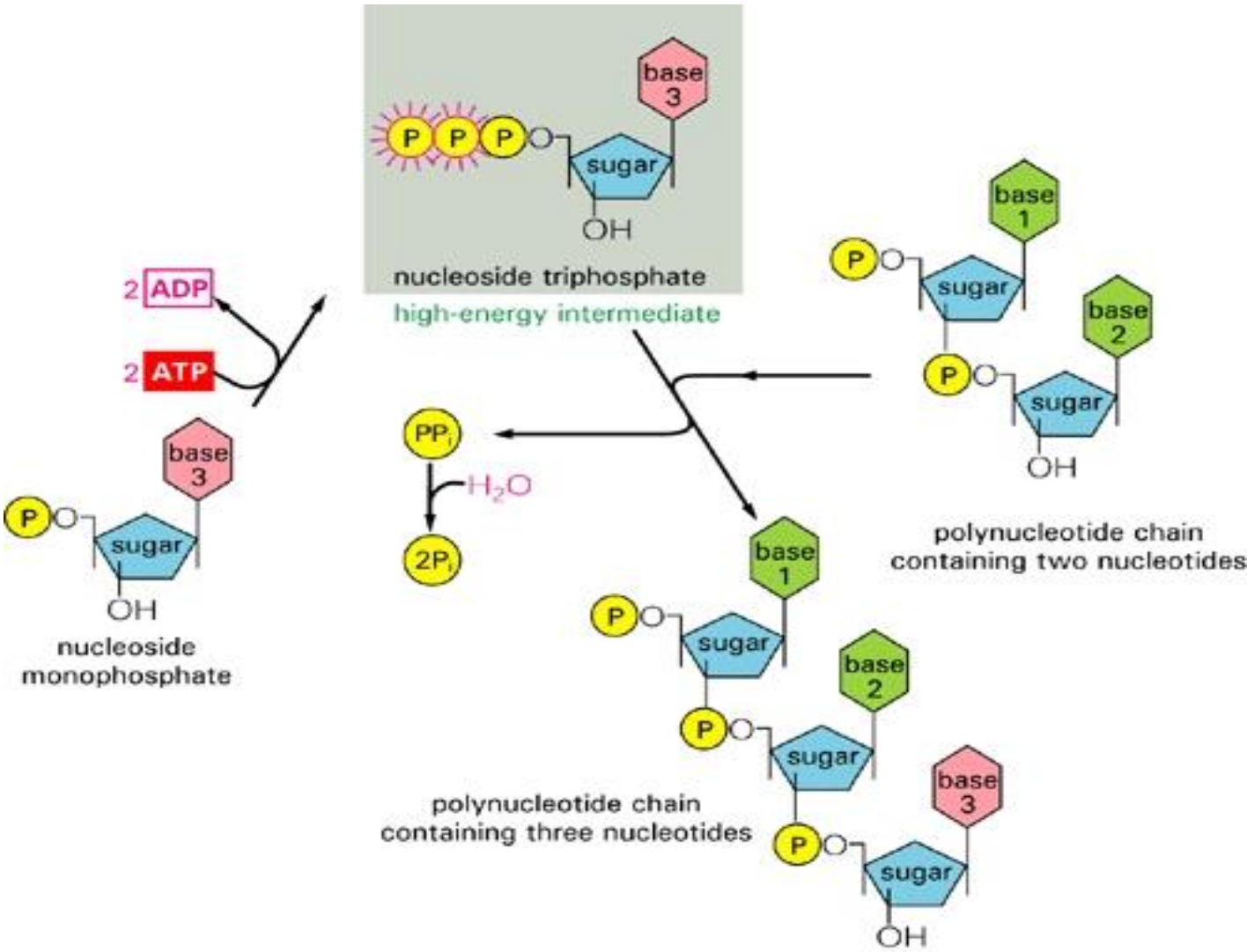
GGCAGCCATTAGGAGATCCGCCGCAGCCAG
CCGTCGGTAATCCTCTAGGCGGCGTCGGTC

Directionality

3’ = end with exposed hydroxyl group

5’ = end with exposed phosphate group

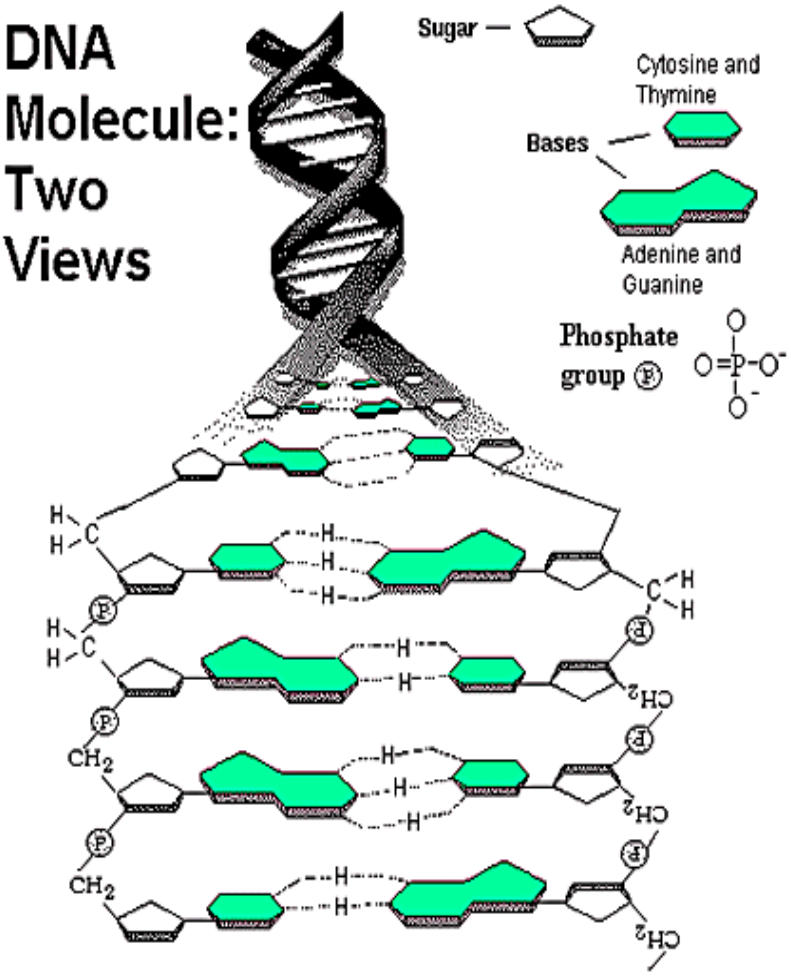




DNA Shape

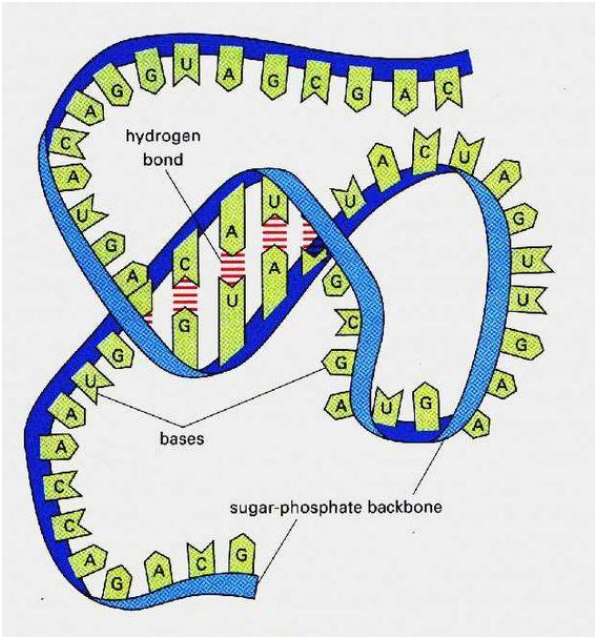
- 2 single strands wrapped around each other = **double helix**.
- Held together **by H bonding** between bases (A-T, G-C)
- Sugars + Phosphates **perpendicular** to bases.
- Strands run **ANTIPARALLEL**. 5 ------ 3

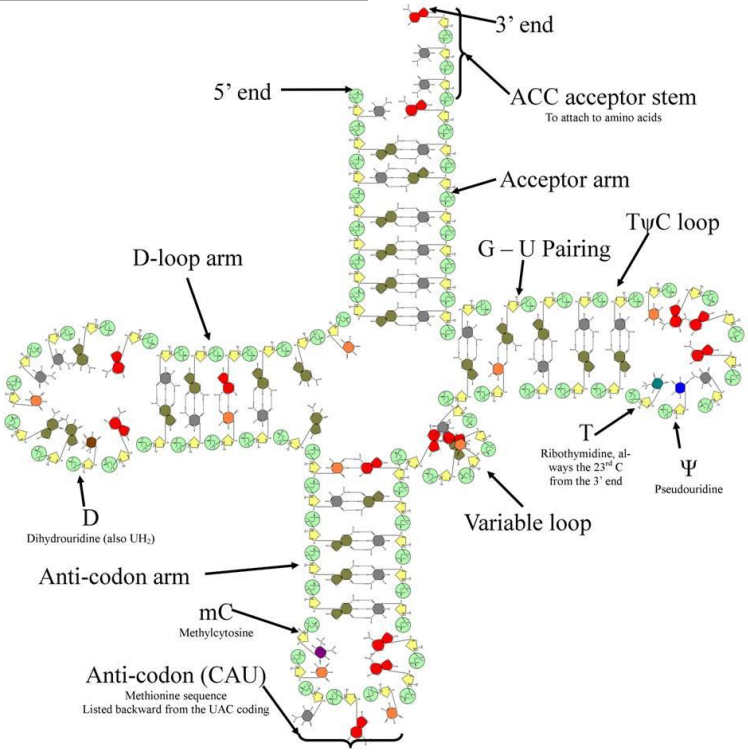
  3 ------ 5

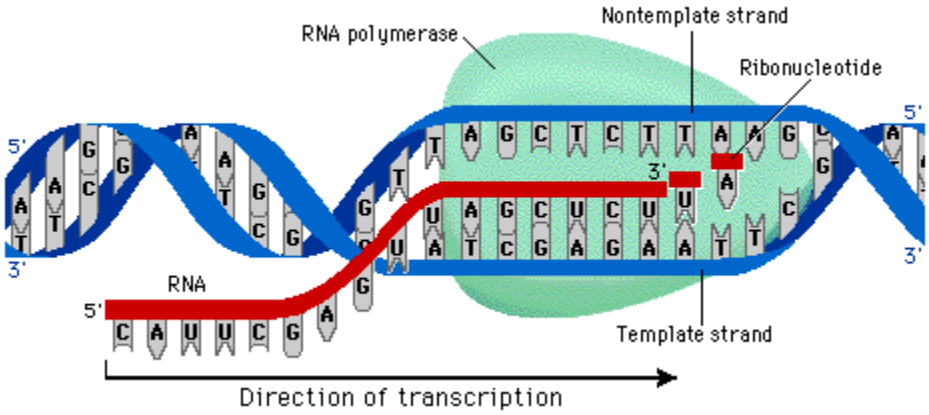


RNA Shapes

- Single Stranded allows a variety of shapes
- Variety of shapes allows variety of functions
  - Ribozymes (RNA enzymes)
  - mRNA (gene sequence code)
  - tRNA (carry amino acids to ribosomes)
  - rRNA (link amino acids)
  - miRNA (degrades specific RNA)
  - siRNA (degrades specific RNA)







RNA is thought to have been the first genetic material rather than DNA. This is known as the 'RNA World' Hypothesis.

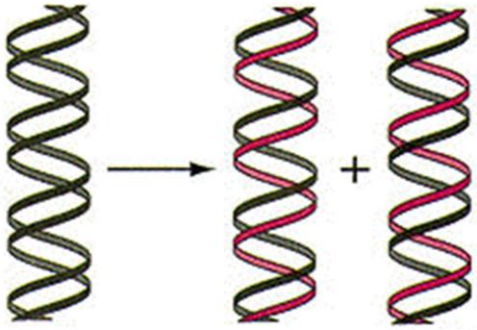
1. Which of the following is least likely to justify the above hypothesis?
    a. RNA is able to catalyze chemical reactions & store genetic information.
    b. RNA can take a variety of shapes allowing numerous functions.
    c. RNA is found throughout various locations in cells.
    d. RNA is more chemically stable than DNA

2. Suppose a scientist were investigating samples of fossil nucleic acids. Which of the following observations would best elucidate the type of nucleic acid?
    a. The amount of hydrogen bonding.
    b. The ratio of guanine to cytosine.
    c. Whether or not there was antiparallel orientation.
    d. The nature of the sugar components.

DNA Replication

Semi-conservative replication model

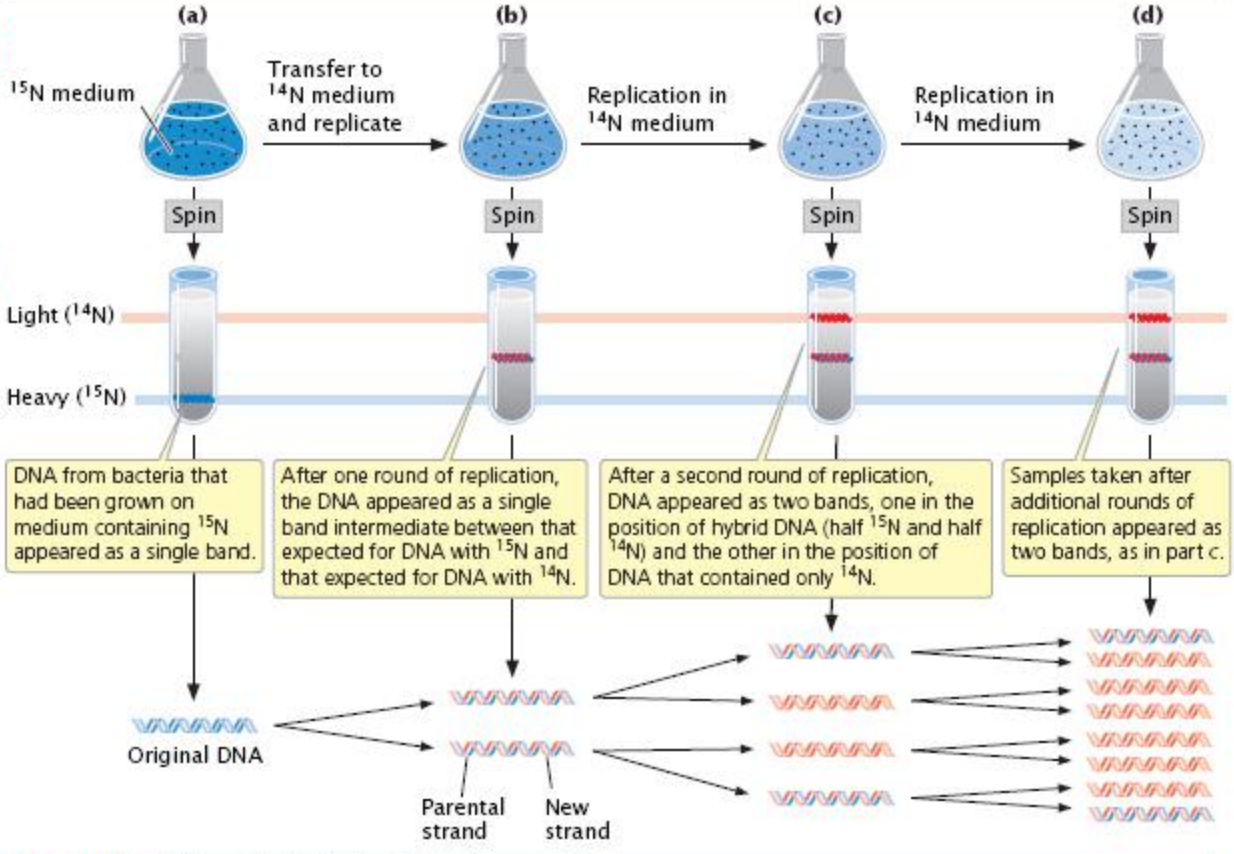
Each **new** DNA double helix has **one old** strand and **one new** strand



Experiment

Question: Which model of DNA replication—conservative, dispersive, or semiconservative—applies to *E. coli*?

Method



Conclusion: DNA replication in *E.coli* is semiconservative.

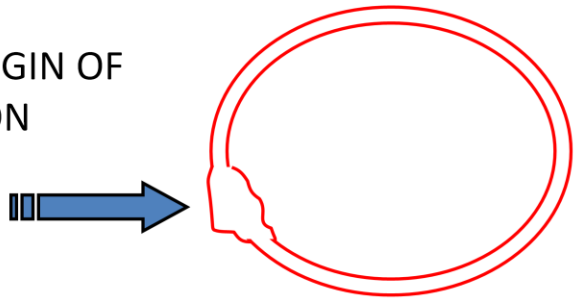
DNA Replication

Prokaryotes

a. **Circular** DNA

b. **Starts** at a **single place**

*Single ORIGIN OF REPLICATION



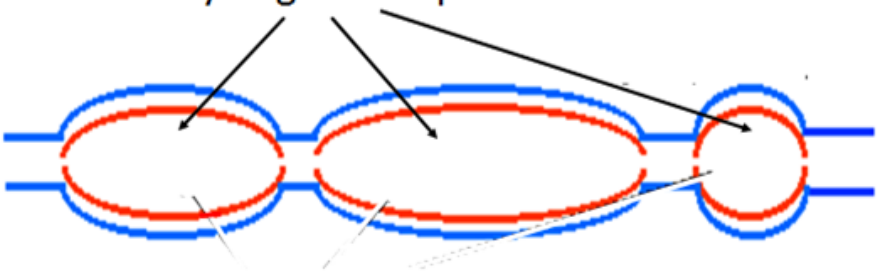
DNA Replication

Eukaryotes

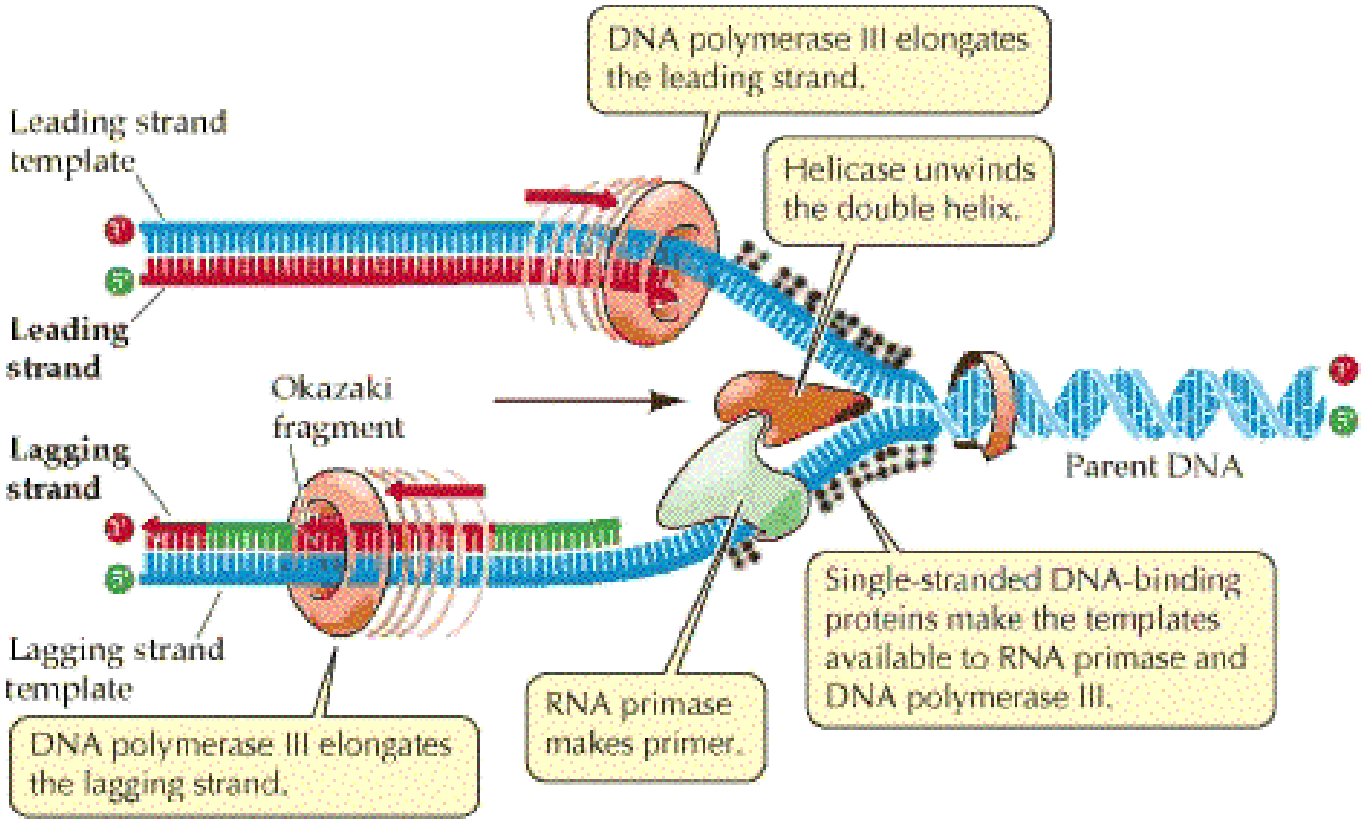
a. **Linear** DNA (Straight line)

b. Starts at **many** places

* many origins of replication



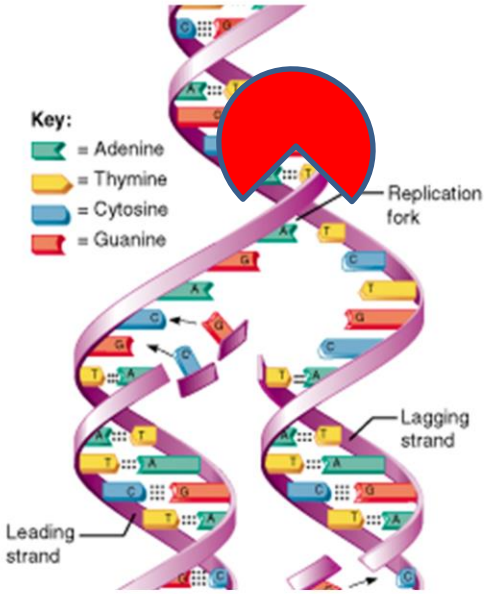
The processes & enzymes involved were first discovered in bacteria. In eukaryotes, the process is a bit more complex. The steps of replication taught here are based on the simple bacteria model.



DNA Replication

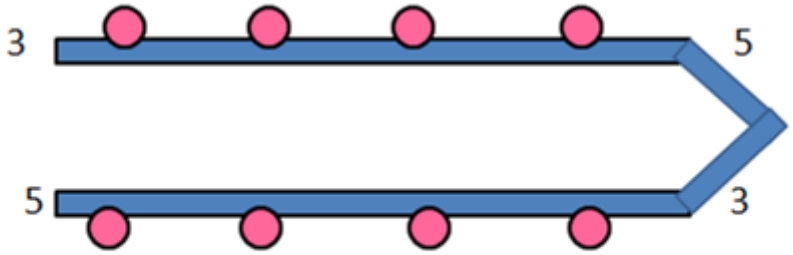
Helicase separates the **2** strands

Each strand becomes a **template** to build from.



Separating the DNA

SSB's hold apart strands, keep hydrogen bonds from re-forming.



Primers

DNA nucleotides must build on existing nucleotides, so a **Primer of RNA** is created by **RNA Primase**.

Leading Strand

Strand that will grow **continuously**

because there is always a free OH to add onto.

Elongates in the **5' → 3'** Direction

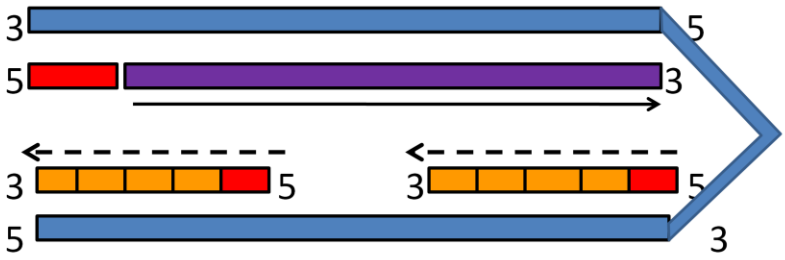
DNA Polymerase adds nucleotides using energy from Dephosphorylation of nucleoside triphosphate (ATP, GTP, CTP, TTP)

Lagging Strand

Strand that will grow **discontinuously**

because the replication bubble keeps opening

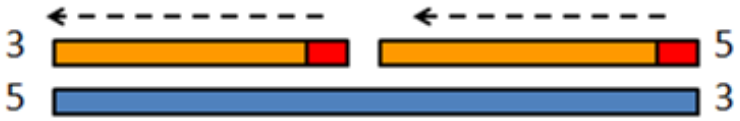
Elongates in the **5' → 3'** Direction *in segments*



Lagging Strand

Each segment = Okazaki Fragment

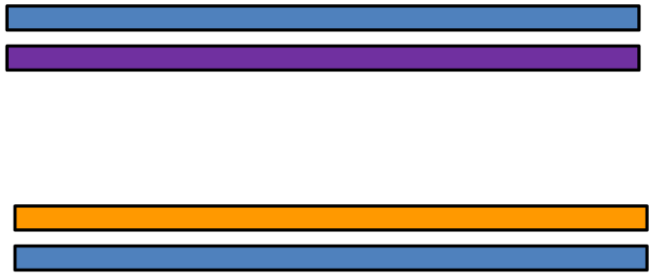
Fragments synthesized DNA polymerase



Removing the Primers

RNA Primers are replaced by DNA

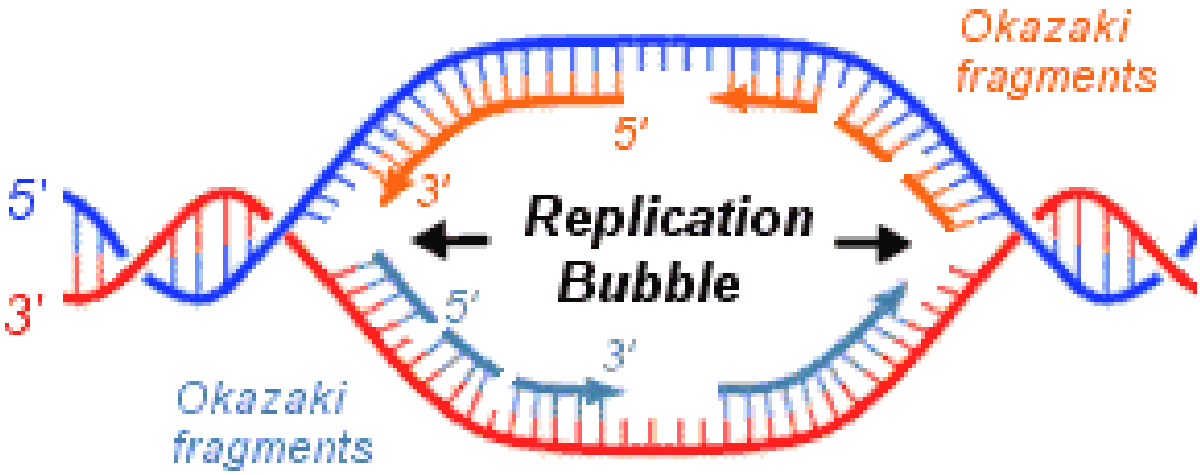
All segments joined by **DNA Ligase**.



Synthesis Summary

The **leading** strand grows _____ the replication fork.

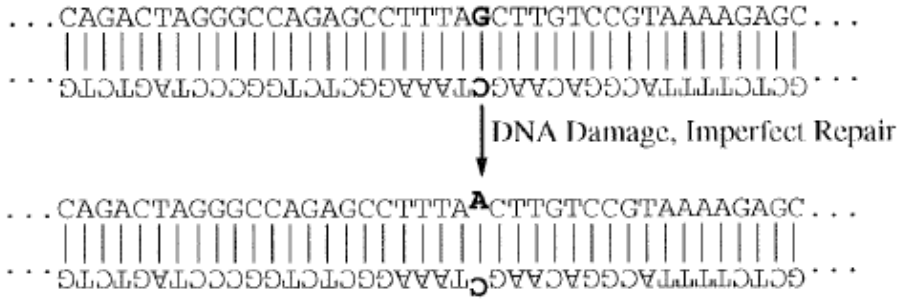
The **lagging** strand grows _____ the replication fork.



1. Which of the following correctly describes the sequence of enzymes used during DNA replication?
    a. SSB's → Helicase → Ligase
    b. Helicase → DNA Polymerase → Primase
    c. DNA Polymerase → SSB's → Ligase
    d. Helicase → DNA Polymerase → Ligase

2. For any given replication bubble, the overall rates of replicating the 2 strands of the unwound double helix must be similar, otherwise areas of one strand would be exposed longer to potentially harmful DNA degrading enzymes subjecting them to higher rates of mutation. Which of the following mechanisms makes the above scenario most possible?
    a. The leading strand must have a faster rate of DNA polymerization than the lagging strand.
    b. The 2 strands must have equal rates of DNA polymerization.
    c. The lagging strand must have a faster rate of DNA polymerization than the leading strand.
    d. Some mechanism must increase the efficiency of Helicase on one strand versus the other strand.

Mutations in DNA are usually caused by chemical or radiation damage to DNA molecules, followed by imperfect repair of the damage. Immediately after this kind of imperfect repair, there may be a mismatched base pair in the DNA. The illustration below shows an example of a mismatch, with the relevant pair bases in bold.



Which of the following best represents the DNA of the two daughter cells produced when a bacterial cell with this particular mismatch replicates its DNA and divides?

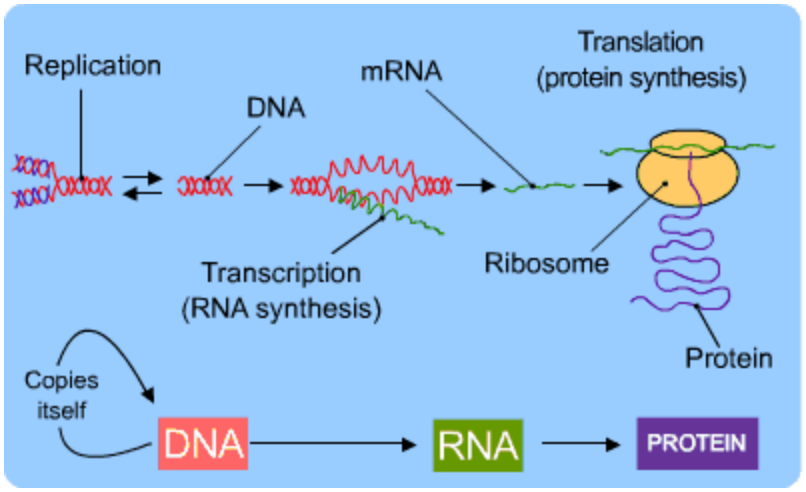
(A)
...CAGACTAGGGCCAGAGCCTTTAGCTTGTCCGTAAAAGAGC...
...GCTGCTTTTTACGGACAACGCTTAAAGGCTGCTGGCCCTAGTCTG... Normal
and
...CAGACTAGGGCCAGAGCCTTTAGCTTGTCCGTAAAAGAGC...
...GCTGCTTTTTACGGACAACGCTTAAAGGCTGCTGGCCCTAGTCTG... Normal

(B)
...CAGACTAGGGCCAGAGCCTTTAACTTGTCCGTAAAAGAGC...
...GCTGCTTTTTACGGACAACGTTTAAAGGCTGCTGGCCCTAGTCTG... Mutant
and
...CAGACTAGGGCCAGAGCCTTTAGCTTGTCCGTAAAAGAGC...
...GCTGCTTTTTACGGACAACGCTTAAAGGCTGCTGGCCCTAGTCTG... Normal

(C)
...CAGACTAGGGCCAGAGCCTTTAACTTGTCCGTAAAAGAGC...
...GCTGCTTTTTACGGACAACGTTTAAAGGCTGCTGGCCCTAGTCTG... Mutant
and
...CAGACTAGGGCCAGAGCCTTTAACTTGTCCGTAAAAGAGC...
...GCTGCTTTTTACGGACAACGTTTAAAGGCTGCTGGCCCTAGTCTG... Mutant

(D)
...CAGACTAGGGCCAGAGCCTTTAACTTGTCCGTAAAAGAGC...
...GCTGCTTTTTACGGACAACGCTTAAAGGCTGCTGGCCCTAGTCTG... Mutant
and
...CAGACTAGGGCCAGAGCCTTTAACTTGTCCGTAAAAGAGC...
...GCTGCTTTTTACGGACAACGCTTAAAGGCTGCTGGCCCTAGTCTG... Mutant

Using the DNA: Protein Synthesis



The DNA structure shows how it copies itself. It does not show how it's information is used.

DNA is like a genetic library - Coded information in the form of genes waiting to be expressed into proteins.

Phenotypes are determined by protein products & their activities.

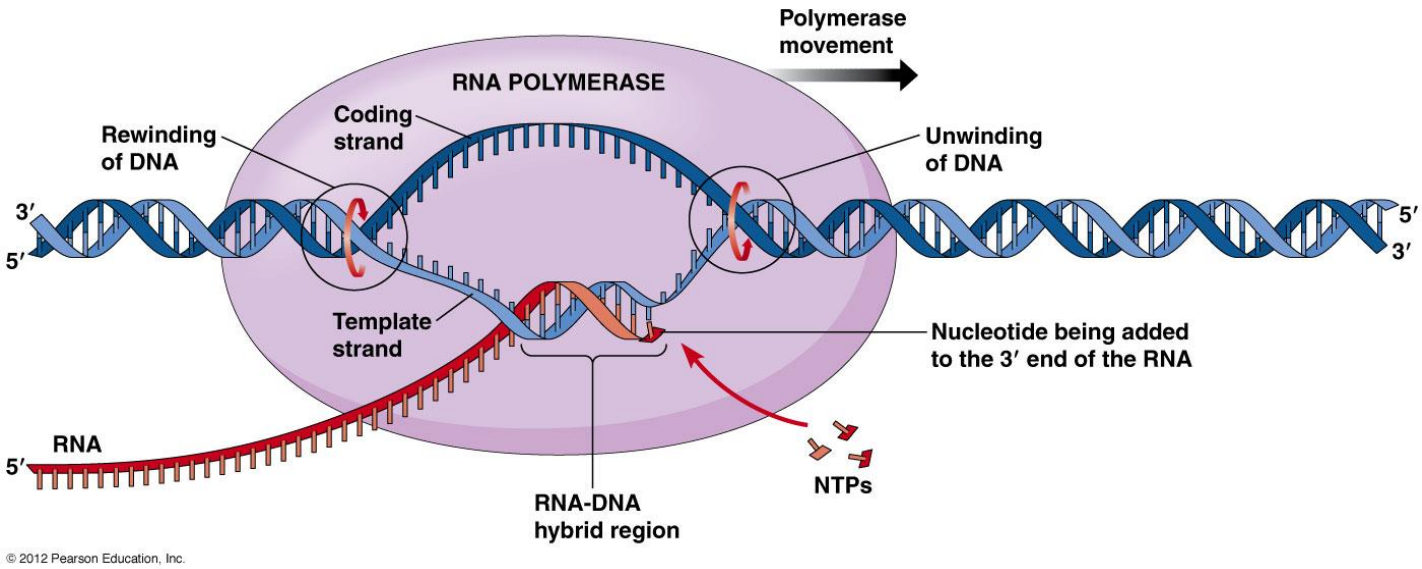
Step 1: Transcription

Transcription Steps

a. **RNA Polymerase** attaches to the **promoter** = signal for where to start.

b. RNA Polymerase unwinds this portion of DNA.

c. RNA Polymerase "reads" the DNA template sequence from 3' → 5' to transcribe mRNA 5' → 3'.



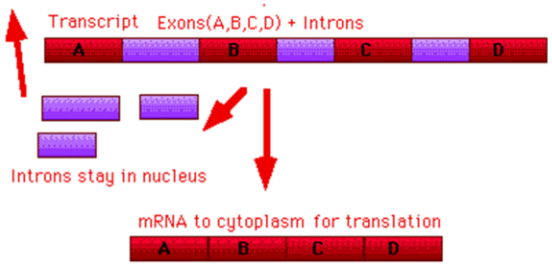
Step 2: RNA Modifications

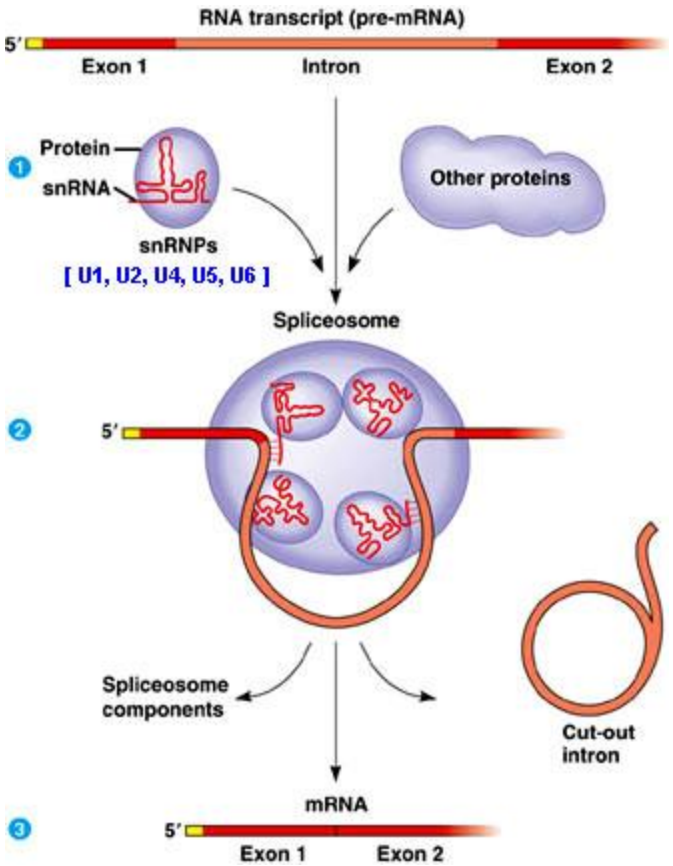
Newly made mRNA has information not needed for making the protein.

a. **Introns**: Not needed for current gene

b. **Exons**: Necessary protein instructions.

Spliceosomes excises the Introns

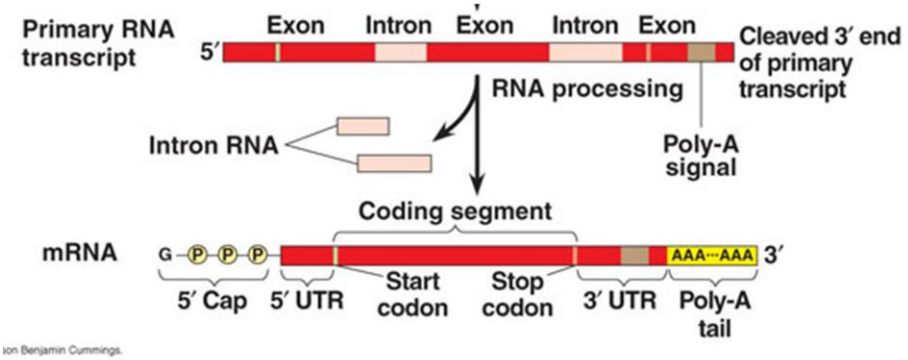


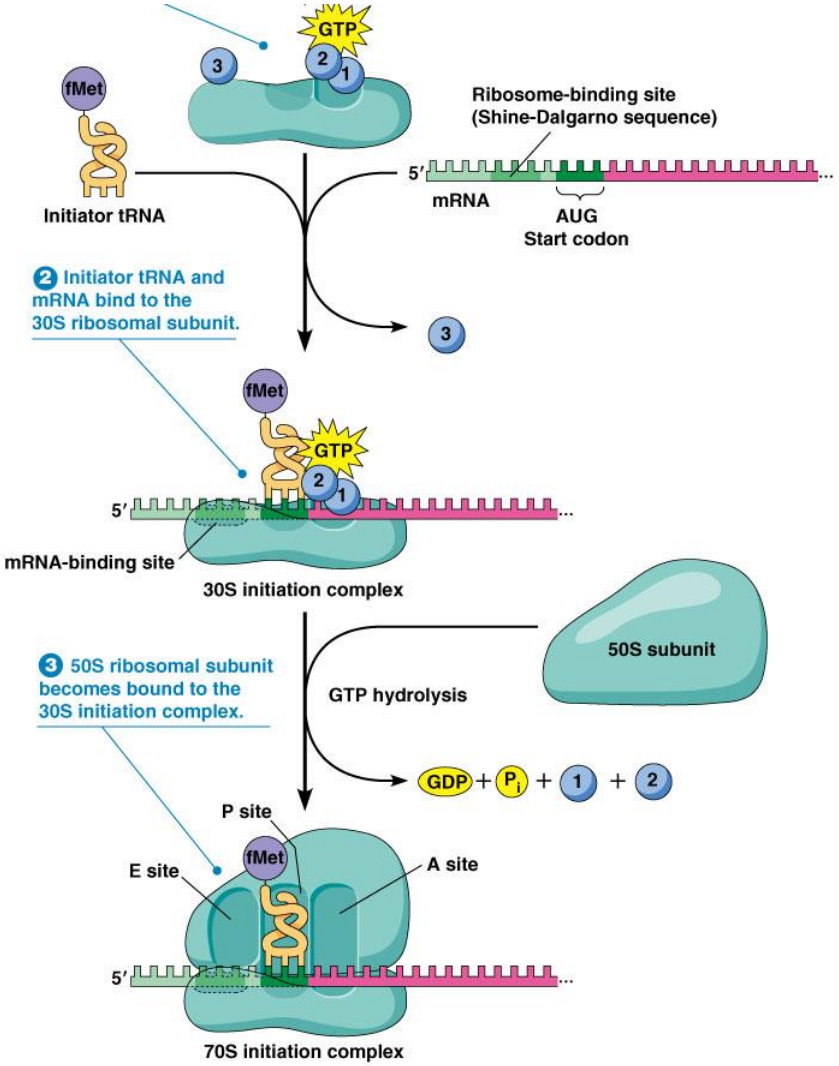


Step 2: RNA Modifications

- Addition of a 3’ poly-A tail
- Addition of a 5’ GTP cap

  *nuclear export, translation, and stability of mRNA





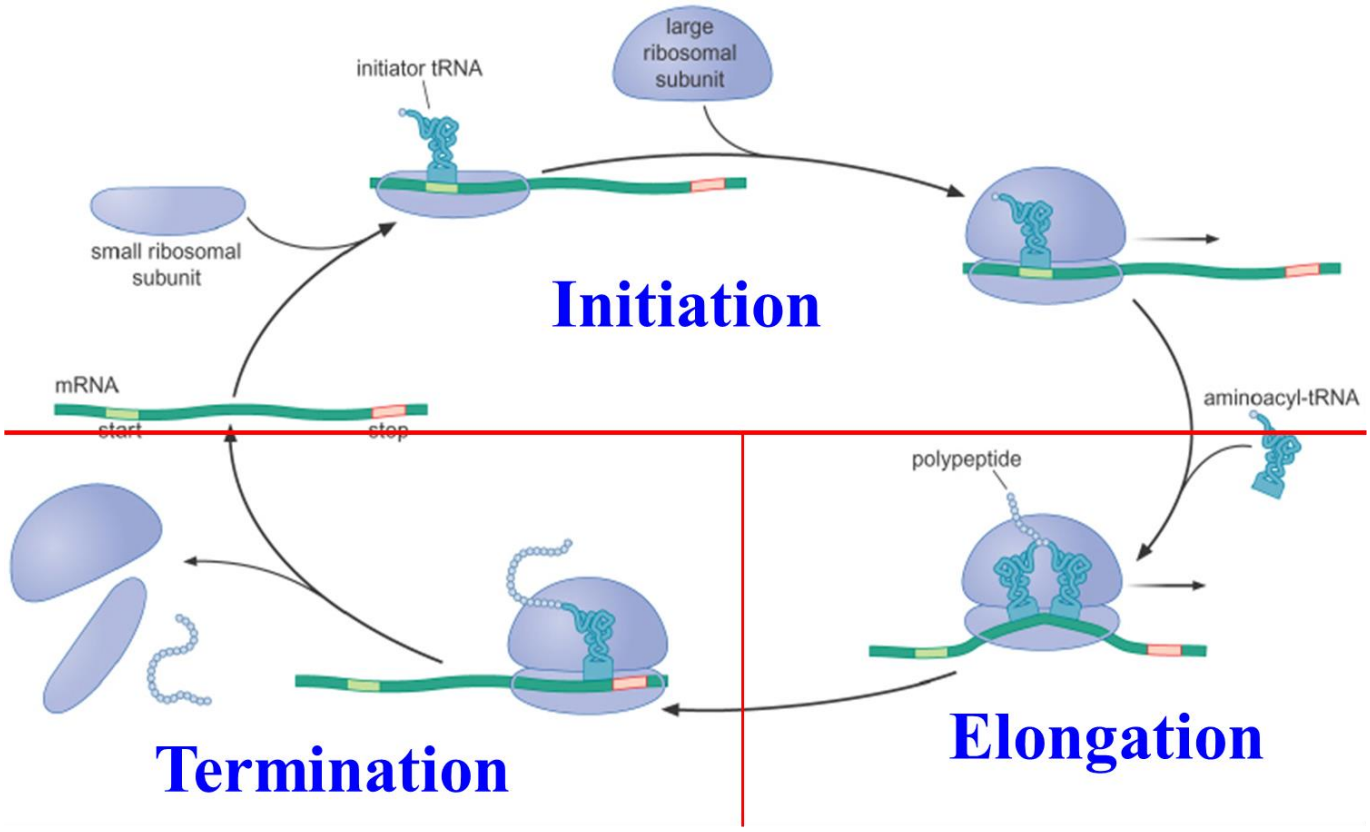
After all modifications are complete, the mRNA leaves the nucleus via nuclear pores, goes into cytoplasm. mRNA then attaches to a ribosome from its 5’ end.

Step 3: Translation

Many steps, but 3 main parts:

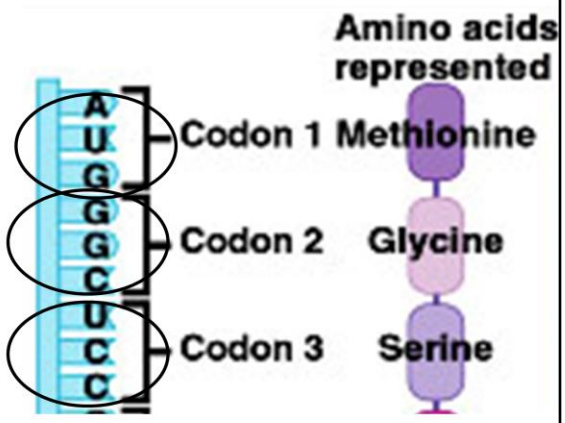
1. Initiation - Signaled by **Start Codon**
2. Elongation
3. Termination - Signaled by **Stop Codon**

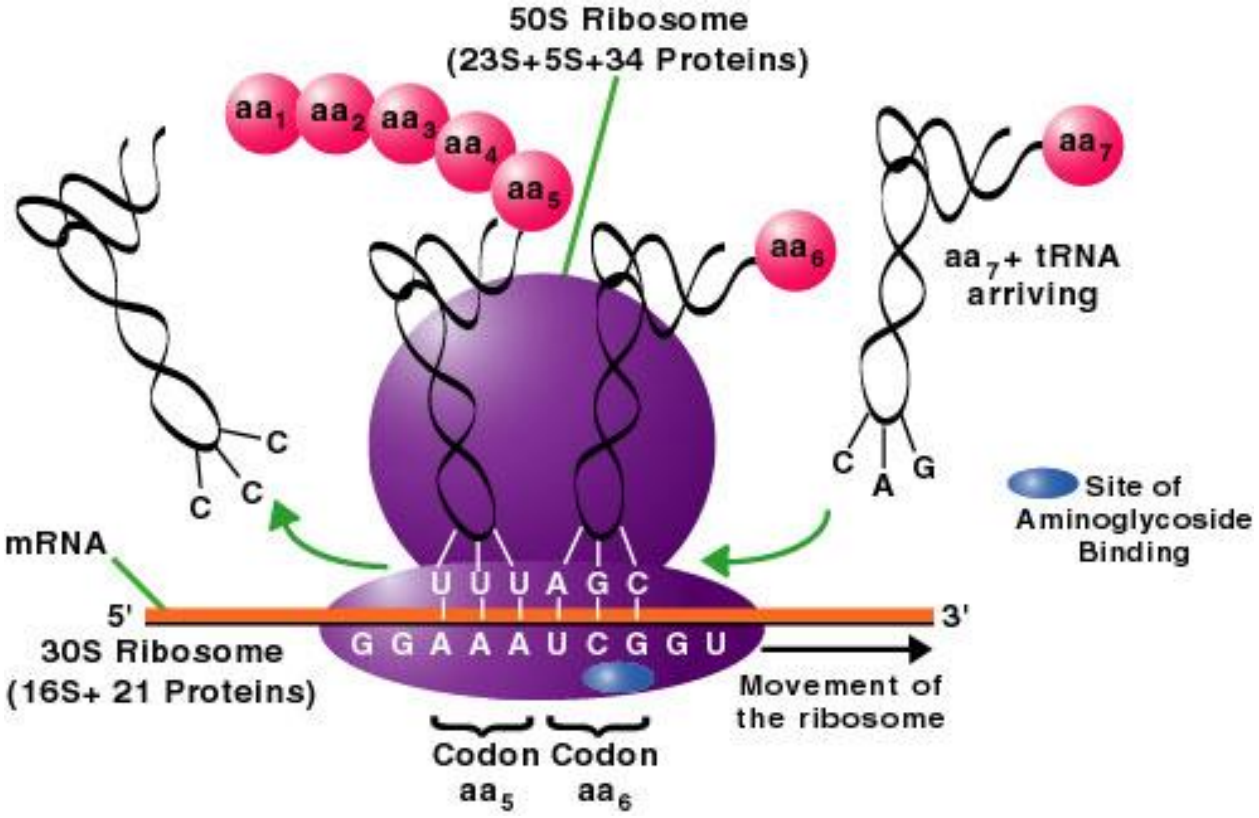
Every protein requires a start & stop codon, so any mRNA sequence will always be **longer** than the actual resulting product.



Step 3: Translation

1. Ribosome is assembled from rRNA & protein, triggered by initiator tRNA
2. mRNA is read in triplets of nucleotide bases called codons





The Genetic Code

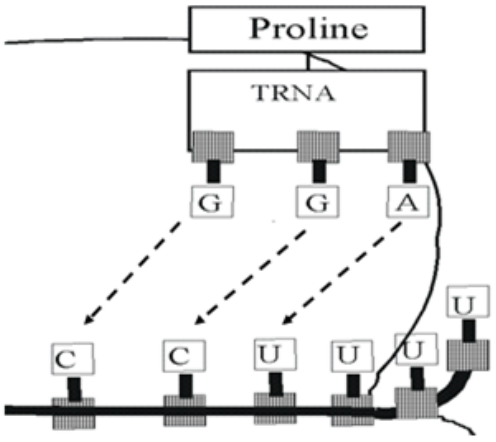
1st letter	Second Letter: U	Second Letter: C	Second Letter: A	Second Letter: G	3rd letter
U	UUU Phe UUC UUA Leu UUG	UCU UCC UCA Ser UCG	UAU Tyr UAC UAA Stop UAG Stop	UGU Cys UGC UGA Stop UGG Trp	U C A G
C	CUU CUC CUA Leu CUG	CCU CCC CCA Pro CCG	CAU His CAC CAA Gln CAG	CGU CGC CGA Arg CGG	U C A G
A	AUU AUC AUA Ile AUG Met	ACU ACC ACA Thr ACG	AAU Asn AAC AAA Lys AAG	AGU Ser AGC AGA Arg AGG	U C A G
G	GUU GUC GUA Val GUG	GCU GCC GCA Ala GCG	GAU Asp GAC GAA Glu GAG	GGU GGC GGA Gly GGG	U C A G

Translation

3. Ribosomes **read** each **codon 5' →3'**

4. **tRNA brings** the matching **amino acid**.

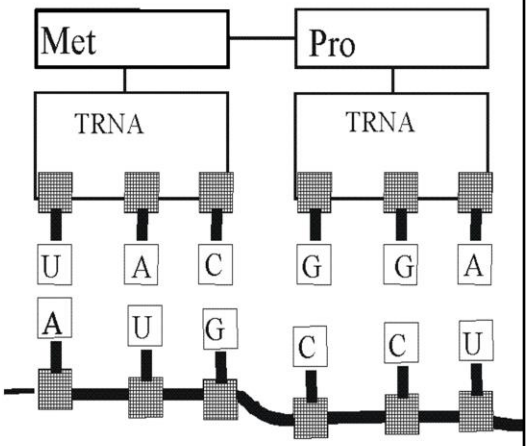
5. Each **tRNA** has an **anticodon** to pair with each **mRNA codon**.

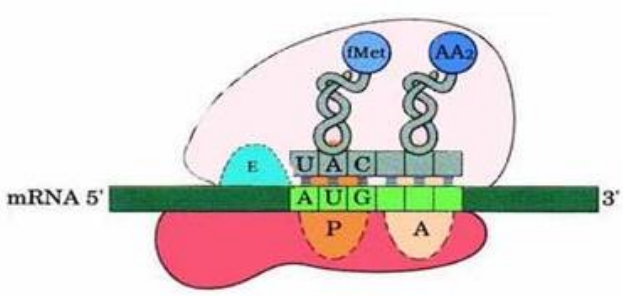


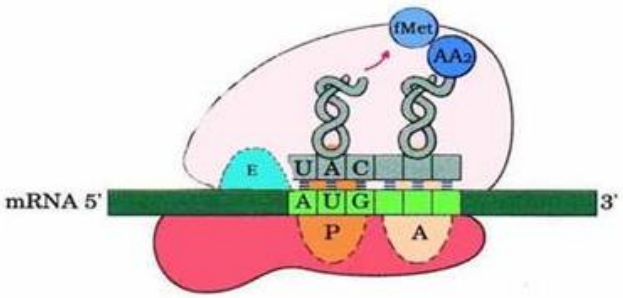
Translation

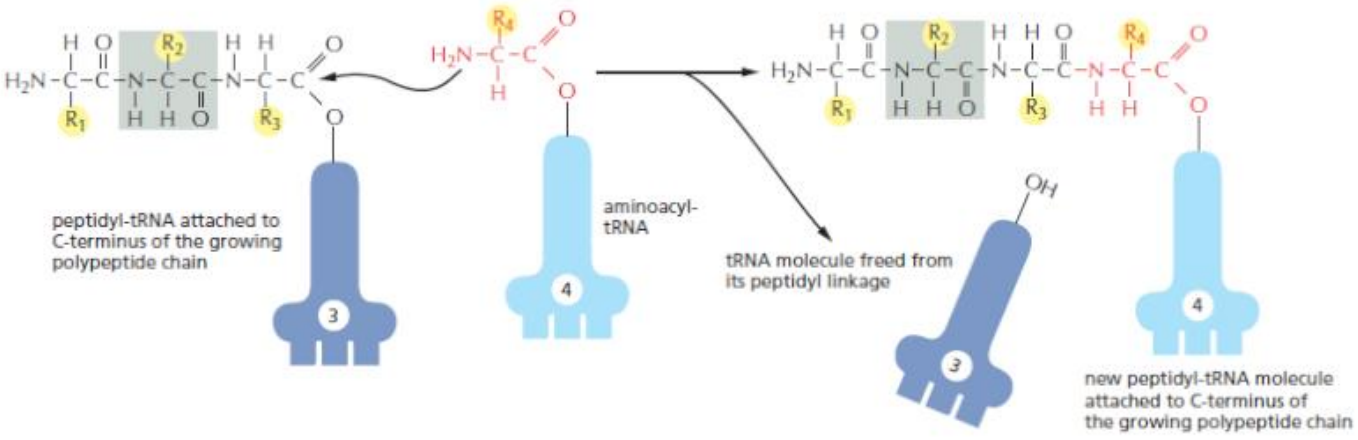
6. **Another** tRNA brings the **next** amino acid.

7. **Peptide Bond** forms **between** the **2** amino acids.



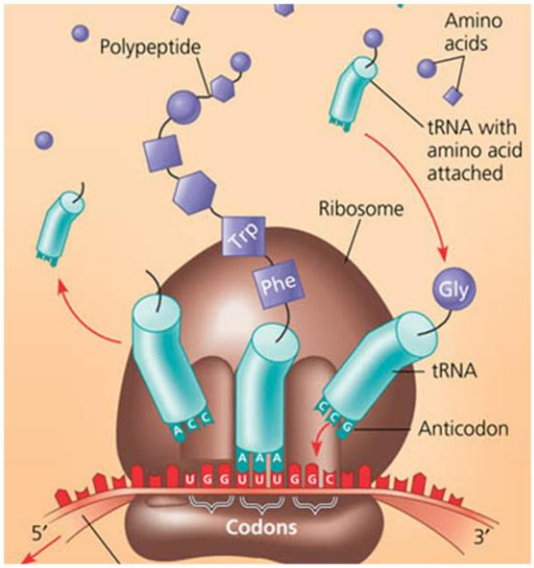






Translation

8. Process **repeats** until **entire sequence** is read, and a "stop" codon is reached. The **protein** is **complete**.



Practice 1: Write the complementary **DNA** strand. Show the correct amino acid sequence result if the TEMPLATE strand is the sequence I provided.

DNA – 3′ TTATGATGCCTGACGACTGCC 5′

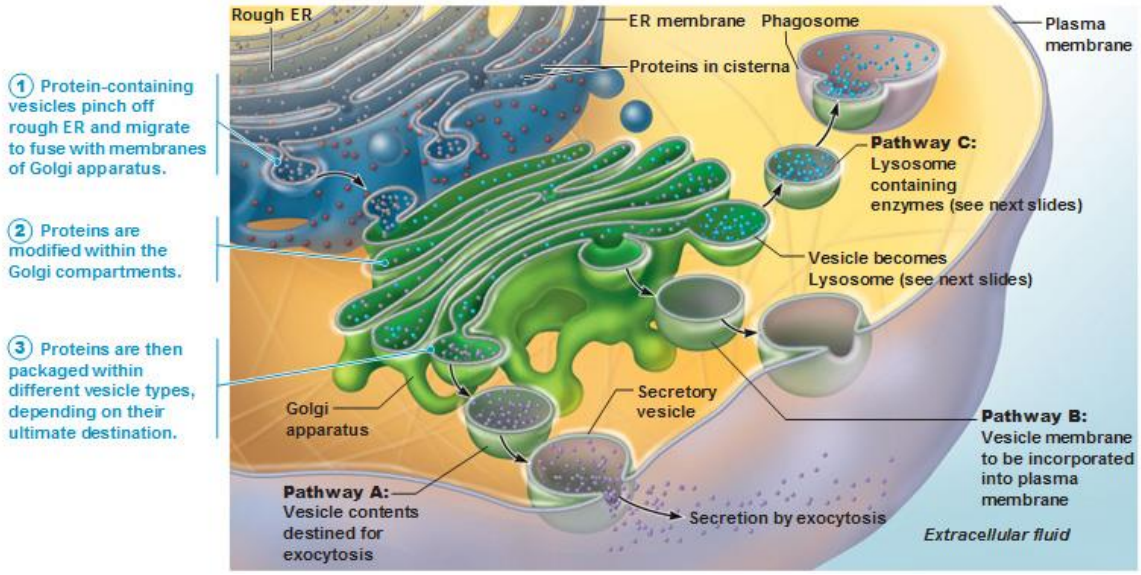
Practice 2: Write the complementary **DNA** strand. Show the correct amino acid sequence result if the CODING strand is the sequence I provided.

DNA – 5′ TTATGATGCCTGACGACTGCC 3′

Destination of the Protein

- **Free ribosomes** in the **cytoplasm** produce proteins that will function within the cell:
  - Metabolic Enzymes (glycolysis, Krebs cycle)
  - Mitochondria/Chloroplasts/Nucleus proteins
- **Bound ribosomes** on the **ER** produce proteins that will be exported from the cell OR that will become part of the ER or Plasma membrane
  - Transport channels - Receptors

The sequence of events from protein synthesis on the rough ER to the final distribution of these proteins.



Prokaryotes…

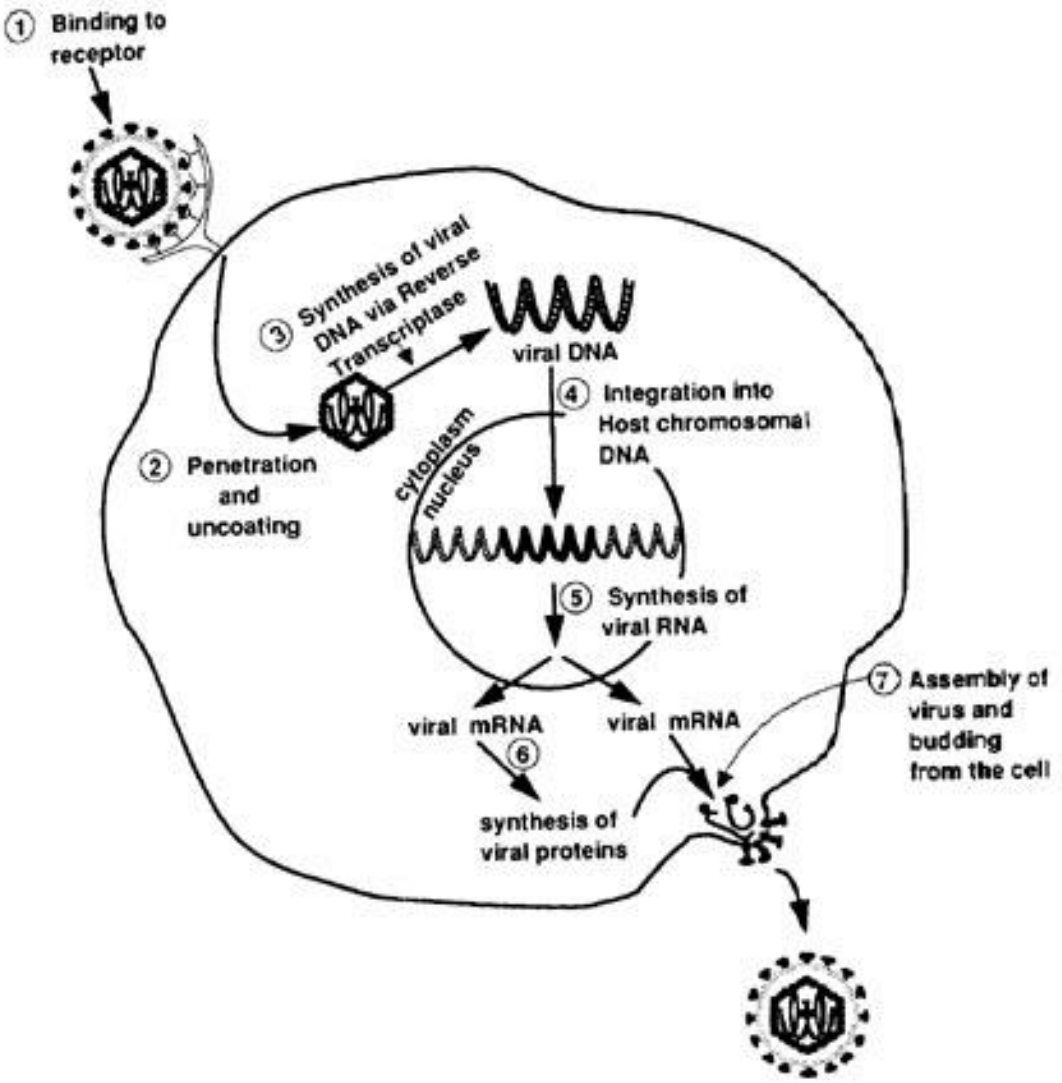
- Transcription & Translation happen in 'lock-step', with transcription coupled directly to translation.
- MUCH LESS regulation of all these processes.
- Otherwise, the sequence of events is similar.

Always an Exception…

- Special scenario: **RETROVIRUSES**
- Alternative sequence: (v = viral h = host)

  vRNA→ **v**DNA →**vh**DNA→**v**RNA →**v**Proteins

  Reverse Transcriptase… quite possibly the scariest yet most amazing enzyme ever to have evolved (in my opinion anyway ☺)
  - Human Immunodeficiency Virus
  - Influenza



1. People with type 1 diabetes lose the ability to transport glucose from their blood into their body tissues for storage. The translocation of glucose requires a transport protein found in the plasma membrane of intestinal cells which is lacking in the membrane of people with type 1 diabetes; however, the transmembrane protein is found in high concentrations within the intestinal cells. Which of the following best models the most likely defect in the pathway?
    a. Transcription is blocked due to a genetic defect in the intestinal cell DNA.
    b. tRNA molecules ae defective due to a genetic defect in the intestinal cell DNA.
    c. Factors that signal packaging of the protein into vesicles are blocked.
    d. Factors that signal ER ribosome formation are blocked.

2. If the transport protein required for glucose translocation is 36^2 amino acids long, what is the minimum number of codons that would be present on the corresponding mRNA?
    a. 1,296
    b. 1,298
    c. 3,888
    d. 3,894

I. DNA Changes

- WHY does DNA change?
  - Errors in replication or repair mechanisms
  - Radiation/Reactive chemicals
  - DNA transfer mechanisms
- HOW does DNA change?
  - Single base (A to G)
  - Additions/Deletions/ Inversions/ Translocation of entire sequences
  - Entire chromosome deleted/added

The phenotypic result of a mutation depends on the environment.

Some mutations will lead to new, favorable traits.

Other mutations will lead to bad, deadly traits.

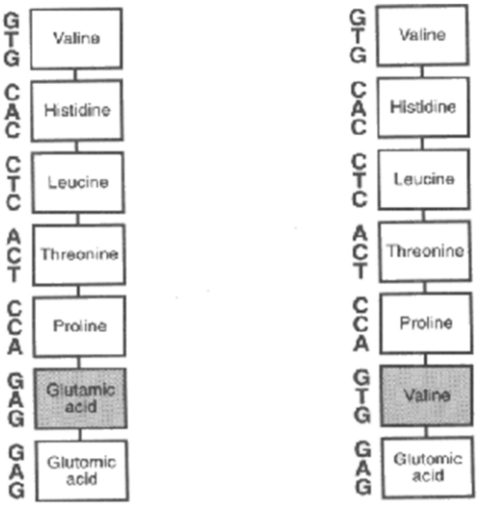
And still others will have no effect.

In the end, mutations are the PRIMARY source of genetic variation for NS to “choose” from.

Mutations

a. Substitutions: **Replace** 1 base with a **different** one.

Sickle Cell Anemia
- Hemoglobin

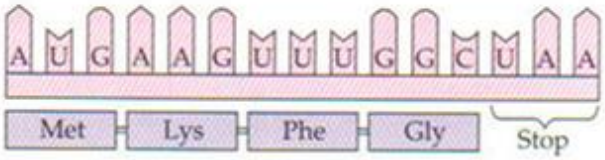


Mutations

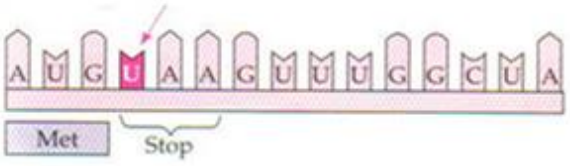
b. Insertions: **Add** a base or codon.

Muscular Dystrophy (Dystrophin)

Original



Result

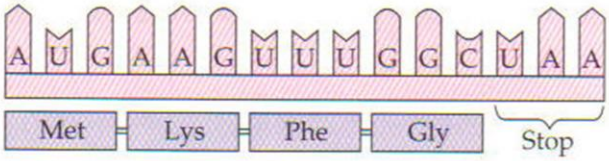


Mutations

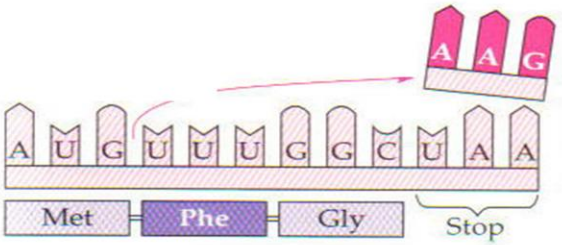
c. Deletions: **Remove** entire **codon**.

Prader-Willi Syndrome

Original

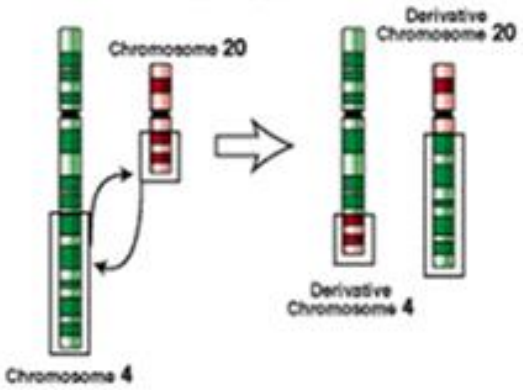


Result 1



Mutations

d. Translocation: **Part** of one **breaks** off and **attaches** to another. (MEIOSIS)



Viruses Transfer DNA

- This is called **TRANSDUCTION**
- Many viral infections involve a virus inserting ITS DNA into the HOST'S DNA, thus changing the host genome.
- Otherwise, the viral DNA may remain in the body, perhaps taken up later on.

This is why viral diseases can be so difficult to detect before it's too late.

Many times, the virus can never be removed from the body and can cause symptoms at any time.

HSV & HPV remain in certain cells of the body for life, and can produce symptoms off and on in some infected people.

Virus Categories

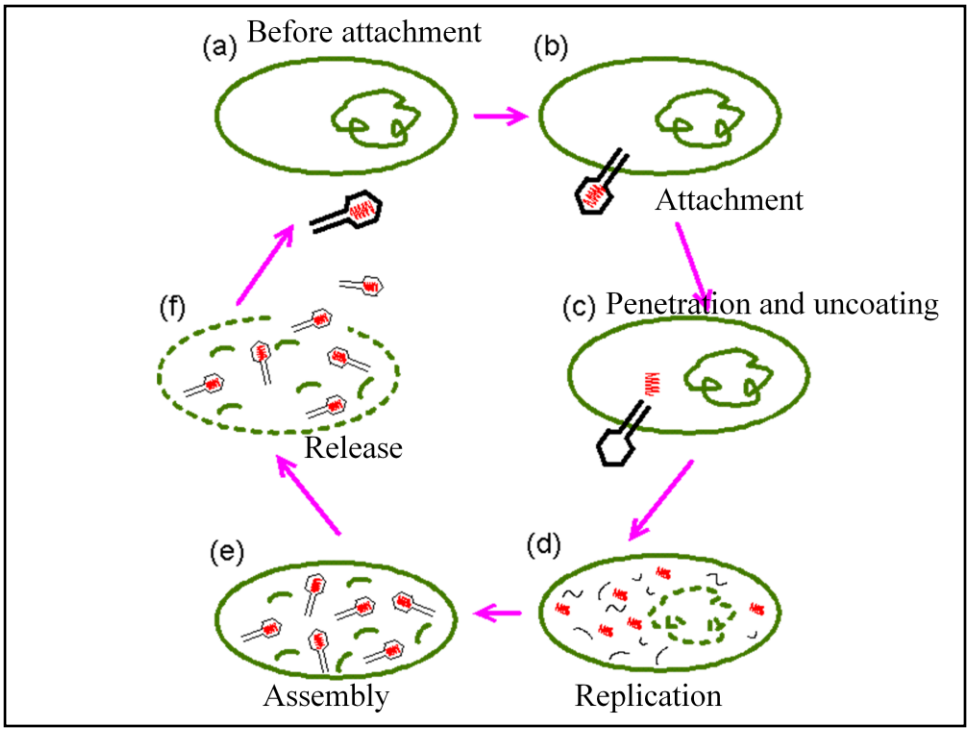
- DNA viruses – stable, do not mutate rapidly
  - Single-stranded or double-stranded
  - Smallpox, Hepatitis B
- RNA viruses – mutate rapidly, unstable
  - ***No error-checking mechanisms***
  - Single-stranded or double-stranded
  - HIV, Rhinovirus

Viral Reproduction

Can only reproduce **inside** a host cell.

Process of reproduction =

Lytic Cycle / Lysogenic Cycle

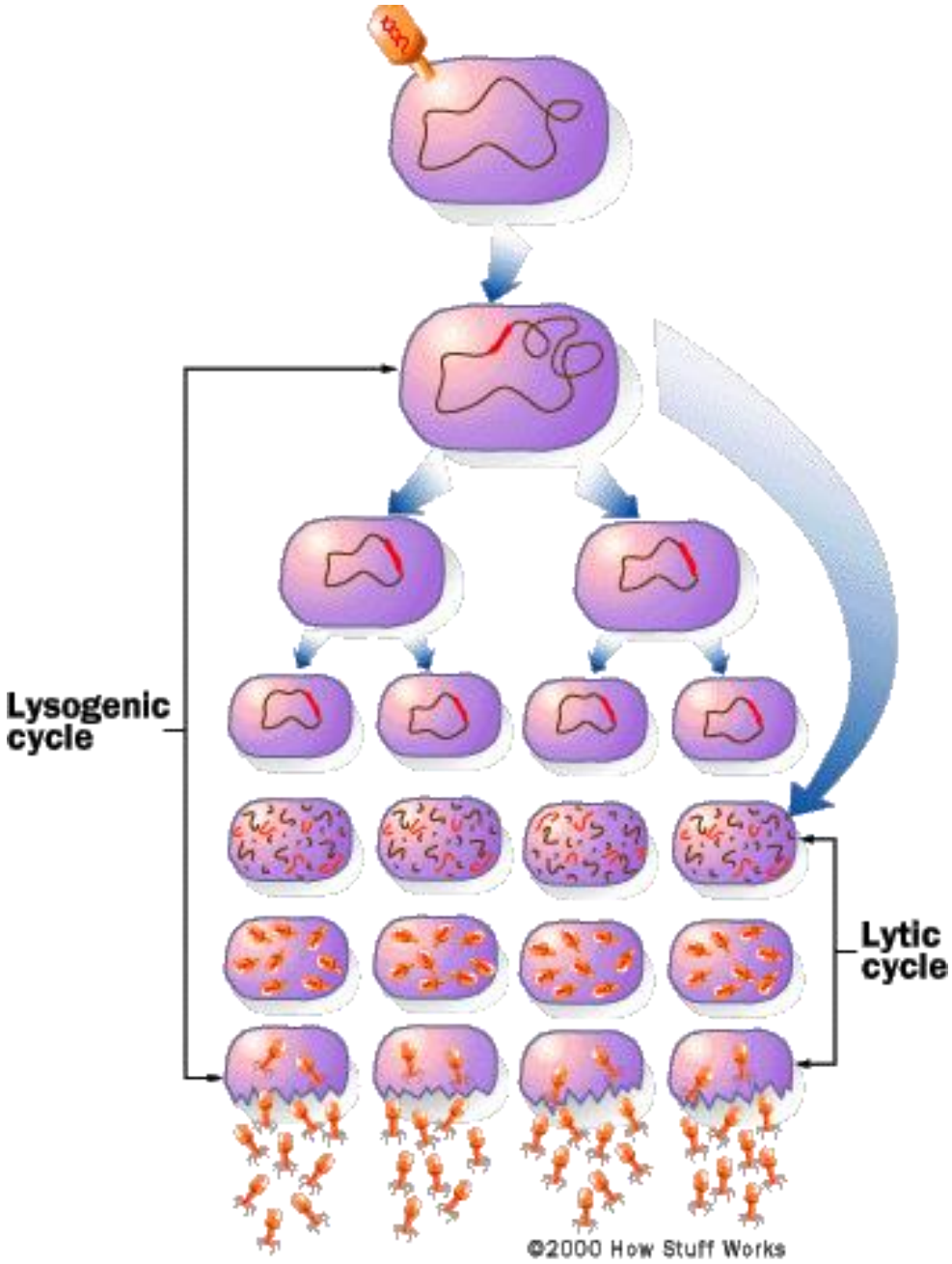


Lytic Cycle

Virus attaches to host cell's membrane and injects its nucleic acid (N.A.)into the host cell.

The viral nucleic acid **takes over protein synthesis,** creating new viruses.

The host cell bursts, lyses, releasing the newly formed viruses.



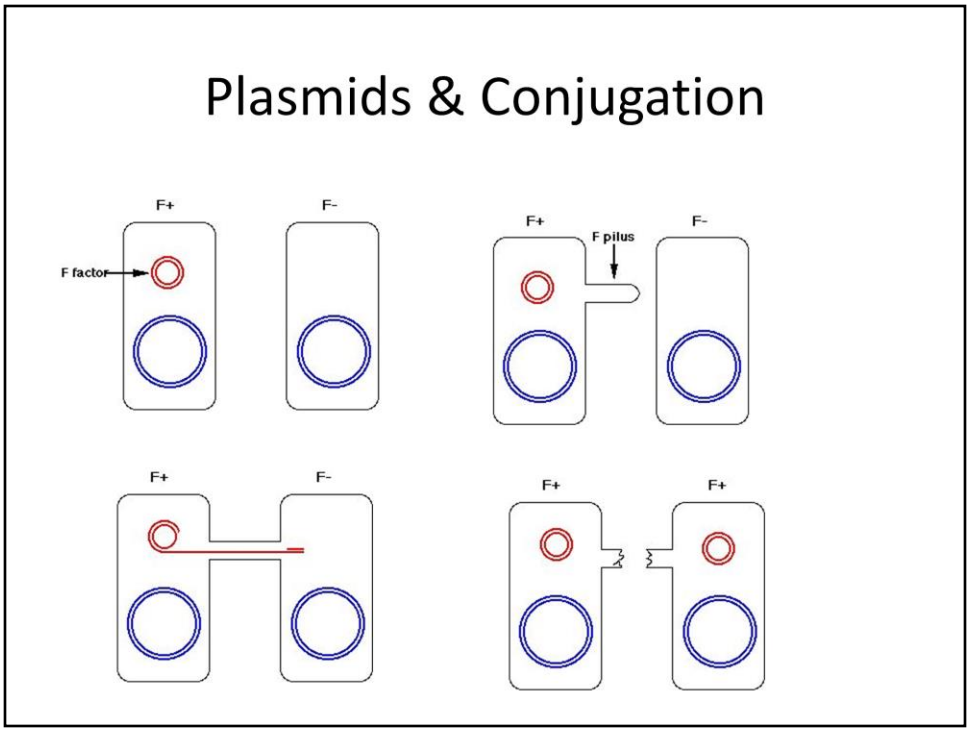
Lysogenic Cycle

The virus injects its N.A. into a cell.

The virus N.A. **attaches** to the cell's DNA

The combined N.A. will **replicate** many times.

The virus N.A. begins the **lytic** infection cycle.



Plasmids: Circular pieces of DNA in bacteria

Exist and replicate independently of genome.

Not essential for bacteria.

Conjugation: Discovered in 1947 by Lederberg and Tatum

Definition: A plasmid or other DNA element is transferred from one cell to another through direct contact (one-way).

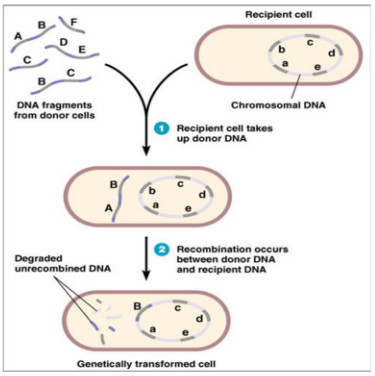
Donor: Cell that provides genetic material

Recipient: Cell that receives genetic material

Inconclusive evidence as to whether bacteria can transfer DNA to other non-bacterial species naturally.

Transformation

Transformation: A cell **takes in** DNA from **outside** the cell. This **new** DNA becomes **part** of the cell's DNA.



Natural Transformation

Only some bacteria can take up free DNA naturally:

- Genetic exchange
- DNA repair
- DNA as food

Artificial Transformation

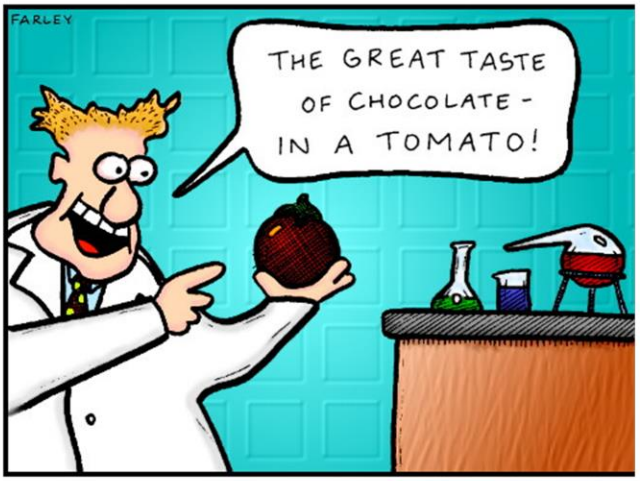
Humans manipulate bacterial cells to make them more "likely" to take up DNA and become transformed.

1. A patient visiting a doctor for an unknown disorder is asked a variety of questions by the doctor. Which of the following questions is least likely to pinpoint the reasoning behind the patient's disorder?
    a. Have you been exposed to any radiation or mutagenic chemicals?
    b. Have you had any bacterial infections in the past?
    c. Have you had any viral infections in the past?
    d. Do any genetic disorders run in your family?

Artificially Manipulating DNA

Genetic engineering: Changing the DNA code of living things.

a. Sequence DNA
b. Edit DNA
c. Put DNA into organisms



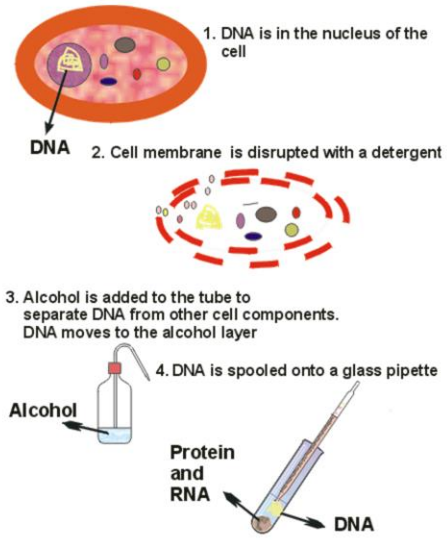
What we have to look forward to from genetic engineering.

Manipulating DNA

1. DNA extraction

   a. Break open cells.

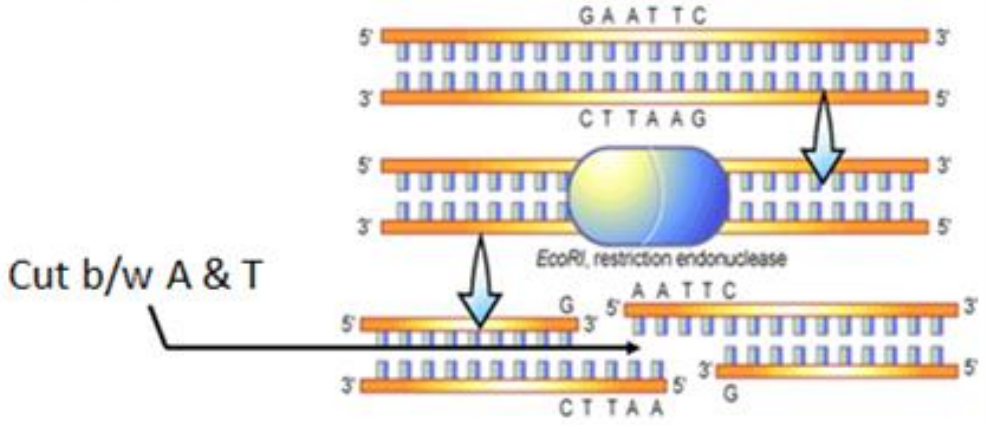
   b. Separate DNA from everything else.



Manipulating DNA

2. Cutting DNA

   b. Use **restriction enzymes**: Cut DNA at **certain** places.



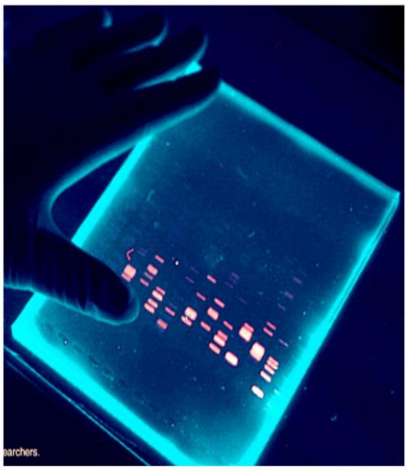
Manipulating DNA

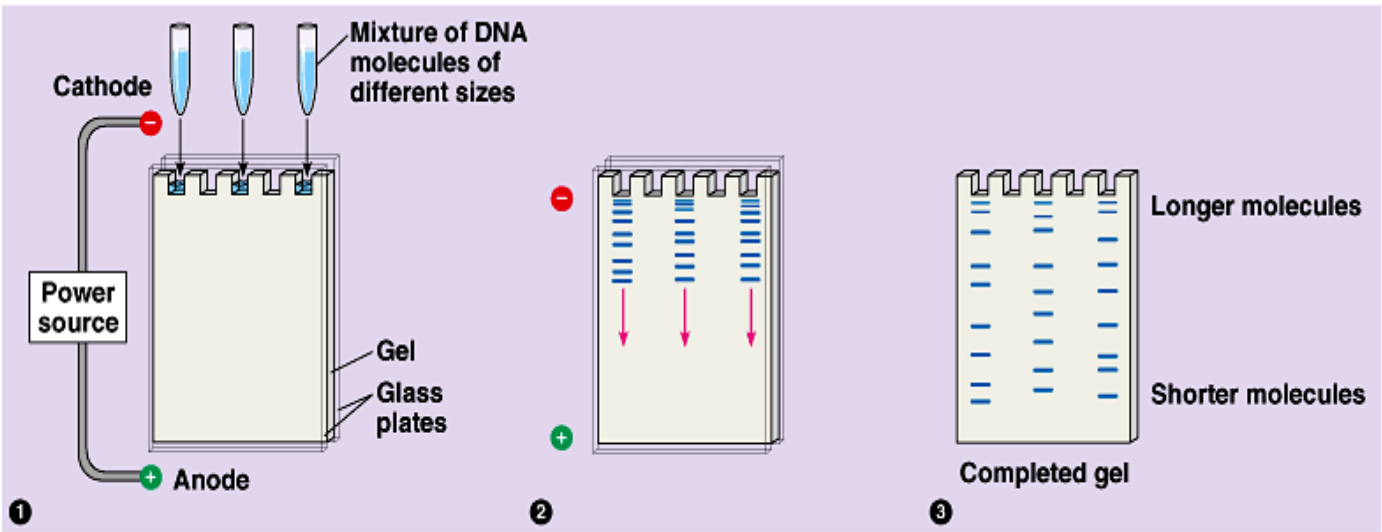
3. Separating DNA

a. Gel electrophoresis

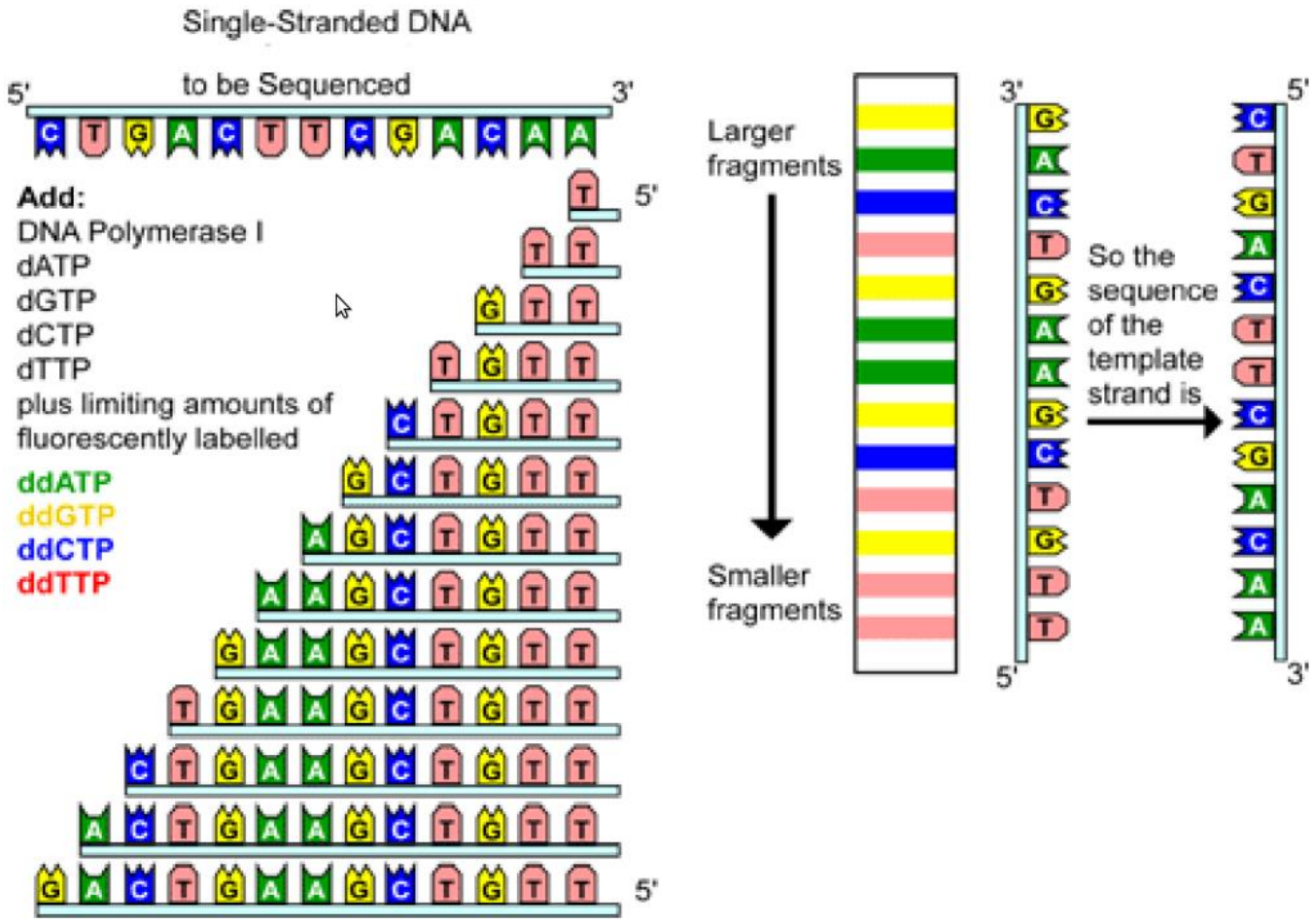
Separates DNA fragments.

Shows similarities & differences between organisms' DNA.



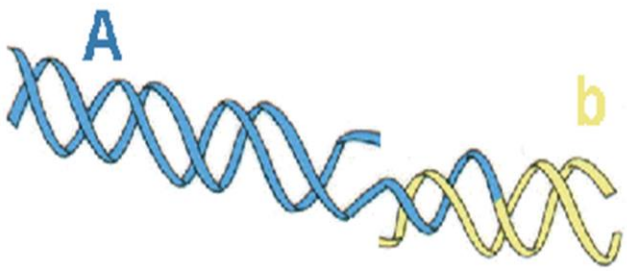


Sequencing the DNA



Using The DNA Sequence

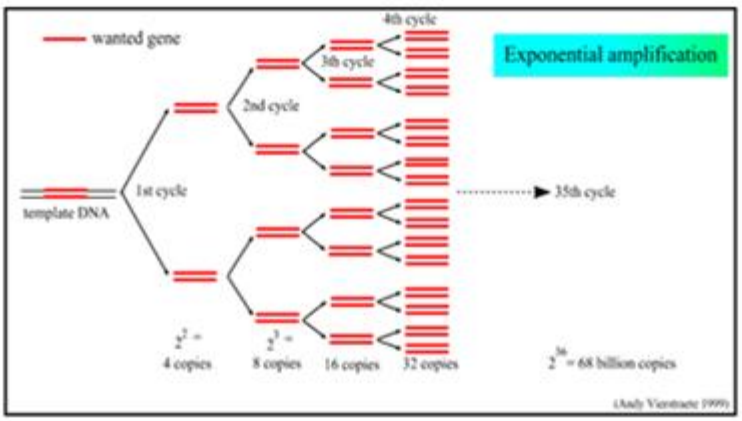
1. Gene Splicing: Combines DNA from 2 different sources.



Using The DNA Sequence

2. Copying DNA

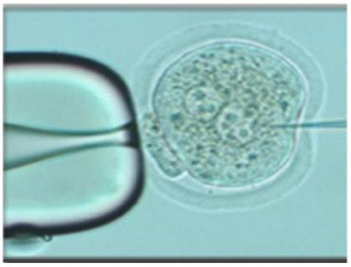
   a. Polymerase Chain Reaction (PCR)= Makes many copies of a gene.



Useful Applications

Transgenic organisms: Have **genes** from **other** species.

Major products of genetic engineering!



Transgenic **microorganisms**

a. **Insulin**, growth hormones

b. Fight **cancer**?

Transgenic **plants**

a. Increased **food supply**

Transgenic **animals**

a. Increased food supply

b. Study **genes**

http://science.discovery.com/video-topics/sci-fi-supernatural/kapow-superhero-science-spider-silk-gene-goats.htm

1. When using biotechnology methods for practical human uses, certain standards of ethics must be addressed. Which of the following is a valid ethical question concerning uses of biotechnology?
    a. Can the methods of gel electrophoresis pose any risks to the organisms they will benefit?
    b. Can the methods of PCR pose any risks to the organisms they will benefit?
    c. Can the introduction of foreign DNA into humans cause any negative affects?
    d. Can the sequencing of DNA be done in a more cost-effective manner?